

**Adherence to treatment of Tuberculosis in patients with TB/HIV  
co-infection on concomitant treatment in Addis-Abeba, Ethiopia**

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## Abstract

**Background:** Non-adherence to treatment poses a challenge to tuberculosis (TB) treatment since it increases the risk of drug resistance, death, relapse and prolonged infectiousness. TB patients co-infected with human immunodeficiency virus (HIV) constitute a large proportion of TB patients in Ethiopia. How being co-infected with HIV as well as concomitant treatment with anti-retroviral therapy (ART) among other things affect adherence to TB treatment has not been studied in Ethiopia, and we did a study to explore this.

**Objectives:** To assess magnitude of default and factors associated with defaulting from TB treatment in patients with TB/HIV co-infection who received concomitant treatment, and to assess co-infected patients' and health professionals' perspectives of barriers and facilitators of TB treatment

**Methods:** Through a review of records, we retrospectively assessed the TB treatment outcomes in a cohort of TB patients co-infected with HIV who were initiated on TB treatment in the period July 2006-September 2007 and who concomitantly received ART in three Health Centers in Addis-Abeba. We conducted in-depth interviews with 15 purposefully selected patients and 9 health professionals involved in their management. We also conducted two focus group discussions in patients with TB/HIV co-infection receiving concomitant treatment.

**Results:** We found that, from the 248 patients included, 148(59.7%) completed treatment, 32(12.9%) were cured, 31(12.5%) died, twenty six patients (10.5%) defaulted treatment, 3(1.2%) failed and 8 patients (3.2%) were transferred out. Multiple regression analysis showed that male sex (AOR= 2.66(95%CI: 1.05- 6.71), P=0.038), lower education (AOR= 3.81(95% CI: 1.38- 10.52), P= 0.009), and timing of ART initiation were associated with defaulting from TB treatment, with those started on ART in the intensive phase having the highest risk of defaulting (AOR= 9.68(95%CI: 2.71- 34.57), P= <0.001, as compared to those initiated on ART in the continuation phase), followed by those

initiated on ART before anti-TB initiation (AOR= 4.83(95% CI:1.19- 19.83), P= 0.025, as compared to those initiated on ART in the continuation phase) . The qualitative study further showed that many misperceptions exist among patients about TB/HIV, and that adverse perception of prognosis of TB in the presence of HIV with an eagerness to survive, support from families and health professionals were positively influencing treatment, whereas side effects, pill burden, economic constraints, lack of food, stigma, lack of adequate communication with health professionals and poorly organized TB/HIV collaborative activities were acting as barriers to treatment.

**Conclusion:** The default rate from TB treatment among patients who are TB/HIV co-infected and who received concomitant treatment is still higher than the World Health Organization recommended rate, and many of those who finish treatment seem to face many difficulties. Health professionals and policy makers should be aware of factors influencing TB treatment in these patients and act accordingly, since many of these factors are amenable to change.

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## Abbreviations

<b>AAHB</b>	Addis-Abeba Health Bureau
<b>AFB</b>	Acid fast bacilli
<b>AIDS</b>	Acquired immunodeficiency syndrome
<b>ANC</b>	Anti-natal care
<b>ART</b>	Anti retroviral therapy
<b>CO</b>	Central office
<b>DOTS</b>	Directly observed treatment short Course
<b>EPI</b>	Expanded program for immunization
<b>HAART</b>	Highly active anti retroviral treatment
<b>HIV</b>	Human immunodeficiency virus
<b>HSDP</b>	Health Sector Development Program
<b>MDR-TB</b>	Multi drug resistant tuberculosis
<b>MOH</b>	Ministry of Health
<b>NGO</b>	Non governmental organization
<b>NTLCP</b>	National Tuberculosis and Leprosy Control Program
<b>PCP</b>	Pneumocystis carini pneumonia
<b>PLWHA</b>	People living with HIV/AIDS
<b>SPSS</b>	Statistical package for the social sciences
<b>TB</b>	Tuberculosis
<b>WHO</b>	World Health Organization



### 1.1. Ethiopia: country profile

#### 1.1.1. Demography

Ethiopia is located in the Horn of Africa, at the cross roads between Africa and the Middle East. The total area of the country is about 1.1 million square kilometers and it is bordered by Djibouti, Eritrea, Sudan, Kenya and Somalia. It is a country with high geographical diversity, and the climate also varies with the topography with temperatures as high as 47 degree Celsius in the Afar depression and as low as 10 degree Celsius in the highlands (1).

Ethiopia's population was estimated to be around 81 million in 2006, with a population annual growth rate of 2.5%. Only 16% of the population lives in urban areas, making Ethiopia one of the least urbanized countries in the world. Ethiopia is the third most populous country in Africa, following Egypt and Nigeria. Ethiopia is comprised of a complex variety of nations, nationalities and peoples and linguistic groups with over 80 different languages constituting 12 Semitic, 22 Cushitic, 18 Omotic and 18 Nilo-Saharan languages being spoken in the country. The majority of the population resides in the highland areas of the country. The main occupation of the settled population is farming, whereas the population in the lowland areas is mostly pastoral, moving from place to place with their livestock, in search for water and grass. The major religions are Christianity and Islam (1).

After ruling by successive emperors and kings until 1974, a military government took over the reign of rule until 1991. Currently, a federal system of government exists and the country is administratively structured into nine regional states (Amhara, Affar, Tigray, Oromiya, Somali, Benishangul Gumuz, Southern Nations Nationalities and Peoples, Harari and Gambela) and two city administrations (Addis-Ababa and Dire Dawa administration council) (1).

### **1.1.2. Economy**

Ethiopia is an agrarian country. Agriculture accounts for 54% of the gross domestic product and accounts for about 90% of the exports. Agriculture also employs 80% of the population. Coffee remains the main export of the country, although other agricultural products are being introduced into the export market.

Ethiopia remains one of the least developed countries in the world. The per capita gross national income was estimated to be US\$110. The Ethiopian currency is the birr, and currently, one US dollar is equivalent to about 11 birrs. Between 1974 and 1991, the country operated a central command economy under the socialist banner of the Derg regime. Since the overthrow of that regime, the country has moved toward a market oriented economy. Economic growth averaged about 5 percent per annum during the period 2000-2005; adjusting for population growth, the average per capita income rose by about 2.1% per annum (1).

### **1.1.3. Health profile**

The health system in Ethiopia remains underdeveloped. The majority of the population resides in the rural areas and has limited access to modern health facilities. The health service coverage remains low and the quality of services available, especially in rural areas, is variable, aggravated by poor transportation (1).

There is a heavy burden of disease with a growing prevalence of communicable infections in the country. Many Ethiopians face disease morbidity and mortality largely attributable to potentially preventable infectious diseases and nutritional deficiencies (2).

No elaborate health policy existed up through the 1950s, but a health policy initiated by the WHO was adopted in the early 1960s. In the mid 1970s, a thorough health policy with emphasis on disease prevention and control was adopted, prioritizing rural areas and advocating community involvement. Under the current administration, another health policy has been set, and to realize the objectives of this policy, the government has established the Health Sector Development Programme (HSDP), incorporating a 20 year

health development strategy, through a series of five year development programs. The program calls for the democratization and decentralization of health services; development of preventive health care; capacity building within the health service system; equitable access to health services; self-reliance; promotion of intersectoral activities; and participation of the private sector including non-governmental organizations(NGOs); and cooperation and collaboration with all countries in general and neighboring countries in particular and between regional and international organizations. Currently, the HSDPIII covering the period 2005/06-2009/10 is in its third year of implementation and thousands of Health Extension Workers have been trained for this purpose (1, 2).

Table 1 Basic health indicators for Ethiopia, Ethiopian Ministry of Health (2)

Total fertility rate:	5.4 children per women in life during her reproductive ages.
Infant mortality rate :	77/ 1000 live birth
Maternal mortality rate:	766 per 100.000 live births
Life expectancy at birth:	50 and 48 years for females and males respectively.
Neonatal mortality rate	41/1000 live births
Under 5 mortality rate	123/1000 live births
Percentage of children under 5 underweight	35
ANC coverage	52.1 %
EPI *coverage	72.6%
Contraceptive Prevalence Rate	15%
Attended Delivery	16.4%

\* Expanded program for immunization

#### **1.1.4. Traditional medicine in Ethiopia**

Traditional medicine was the only system of health care until the advent of modern medicine. Even today, a large majority of the population relies on traditional medicine( in 1991, it was estimated that 80% of the population was using traditional medicine); due to

shortage and inequitable distribution of health services but also due to the persistence of traditional beliefs and practices among the public, and in particular in rural areas (3).

Diverse traditional medicinal practices exist, and traditional medicine is concerned not only with the curing of diseases but also with the protection and promotion of human physical, spiritual, social, mental and material wellbeing. The many categories of traditional medicinal practices dealing with these different aspects of health include: spiritual healing, prevention, as well as curative and surgical practices. The health and drug policies of the Ethiopian Ministry of Health recognize the important role traditional health systems play in health care (4).

### **1.2. Study area: Addis-Abeba**

Addis-Abeba, the Capital City of Ethiopia, is located in the heartland of the Country. It has a population of around 3.6 million. It is divided into 10 administrative sub cities and 99 Kebeles (5).

Addis-Abeba Health Bureau is responsible for both curative and preventive health care of the city under which there are 5 hospitals, 1 public health laboratory and 1 nursing school. There are also 10 sub-city health departments, which are directly accountable to their respective sub-city administration (6).

Totally there are 27 hospitals in the city of which 5 are owned by AAHB, 5 by federal ministry of health, 2 by NGOs, 3 by defense and police and 12 by private owners. There are 24 health centers of which 21 are owned by the city administration, 2 by NGOs and 1 by the public. There are also 456 clinics of which 6 are run by the City Administration, 28 by NGOs and 56 by other government organizations, 46 by factories and 320 by private owners. In addition to these, there are about 180 retail drug outlets and 46 health posts. Moreover, there are about 40 NGOs working in Addis-Abeba on different health activities. Regarding health professionals, there are currently a total of 3,216 professionals out of which 1, 710 are practicing in the public sector under the City Administration and 1,506 in the private sector (6).

The potential health service coverage (the population covered in percentage based on the existing health centers and health stations in catchment's area) in Addis-Ababa with regard to geographical accessibility is 100%, while the primary health care unit coverage is 68 % (6).

The main causes of morbidity and deaths in the City are communicable & nutritional diseases that could be prevented through primary health care activities; HIV/AIDS, TB, and nutritional problems are assuming greater importance. In addition, one of the major problems in the City has now become high rate of accident, i.e. the first in the ten top diseases of Hospital morbidity in the past few years (6).

Table 2 Basic health indicators for Addis-Ababa, Addis-Abeba Health Bureau (6)

Total fertility rate:	2.24 children per women in life during her reproductive ages.
Infant mortality rate :	61/ 1000 live birth
Maternal mortality rate:	566 per 100.000 live births
Life expectancy at birth:	64.1 & 60.3 years for females and males respectively.
ANC coverage	80.4 %
Contraceptive Prevalence Rate	37.8%
Attended Delivery	32.9%
DPT 3	73%

### **1.3. TB, HIV, TB/HIV: pathogenesis, global and national burden**

#### **1.3.1. Tuberculosis**

##### **1.3.1.1. Pathogenesis**

Tuberculosis is an ancient disease. It has affected humans throughout known history and even human prehistory. Robert Koch discovered its causative agent in 1882 and in 1944, the first anti-TB drug, Streptomycin, was discovered. (7) TB is a disease associated with poverty and is responsible for the loss of more years of healthy life than any communicable disease except HIV/AIDS (8). It is the leading cause of death from a curable infectious disease (9).

Tuberculosis is a bacterial disease caused by *Mycobacterium tuberculosis* and occasionally by *Mycobacterium bovis* and *Mycobacterium africanum*. It is transmitted via the respiratory route, with the most important source of infection being the patient with TB of the lung, who is coughing, releasing infectious droplet nuclei, which can also be spread into the air through talking, sneezing, spitting and singing, and can remain in the air for long periods, especially in the absence of direct sunlight (10).

After penetrating the respiratory tract, the bacteria (bacilli) infect macrophages, while CD4+ T-lymphocytes and other lymphocytes produce interferon gamma, interleukin 2, tumor necrosis factor alpha, and macrophage colony stimulating factor, which activate macrophages and cytotoxic cells to inhibit the growth of the bacilli. TB appears when limiting the growth of the bacteria has been impossible for the immune system with insufficient induction of granuloma formation. Interferon gamma formation plays a critical role at this stage (11).

The risk of infection for a person depends on two factors: the extent of exposure to the bacilli and the person's susceptibility to infection. The risk is higher with prolonged and close exposure to an infectious person and in a person with decreased immune function. Of those infected, 90% of people without HIV infection will not develop the disease. Of those with the disease, if untreated, 50% will be dead, 25% will be self cured and 25% will remain ill with chronic infectious TB (10).

### **1.3.1.2 Global burden**

Globally, in 2006, 9.2 million new cases of TB and 1.7 million deaths occurred, of which 0.7 million cases and 0.2 million deaths were in HIV positive people. Mortality due to TB as well as incidence of TB have been decreasing or stabilizing in all regions of the world except Sub-Saharan Africa and, to some extent, Europe (8). In some areas, the factors influencing TB trends remain the traditional ones such as poverty, failures in the treatment system and immigration. In others, and increasingly, the HIV epidemic is playing a major role (12). The 22 high burden countries account for approximately 80% of the estimated number of new TB cases arising worldwide each year, and in developing countries, TB comprises 25% of all avoidable adult deaths (13). Without the implementation of proper control measures, WHO estimates that between 2000 and 2020, nearly one billion people will be newly affected, 200 million will get sick and 35 million will die from TB (14). Tuberculosis affects mainly the economically productive age group with 75% of cases occurring in the age group 15-54 (13).

### **1.3.1.3. National burden**

Ethiopia is one of the 22 high burden countries for tuberculosis, standing 7<sup>th</sup> place in the global rank by estimated number of cases. The incidence of TB in Ethiopia is estimated to be 379 per 100 000 populations for all cases and the prevalence 643 per 100 000 populations (15). According to the MOH hospital statistics data, TB is the leading cause of morbidity, the third cause of hospital admission and the second cause of death in Ethiopia, after malaria (13).

## **1.3.2. HIV**

### **1.3.2.1 Pathogenesis**

The first case of HIV was diagnosed in 1981 and since that period, researchers have identified two serotypes of HIV: HIV-1, the commonest type of HIV worldwide, and HIV-2, most common in West Africa. Both have the same routes of transmission, but HIV-2 is believed to be more easily transmitted, and progression to AIDS might be slower in those infected with HIV-2(10).

The main route of transmission worldwide remains sexual intercourse although the routes of transmission vary greatly between regions. In Sub-Saharan Africa, sexual intercourse, contaminated blood and mother to child transmission play the major role in transmission whereas in the fast growing epidemics in Russian federation and the Ukraine, the commonest cause of transmission is injecting drug use (10).

HIV infects cells which have the CD4 antigen on their surface that is principally the helper T-lymphocytes, which are critical for cell mediated immunity. Thus the principal abnormality in patients with HIV infection results from the fact that the number of CD4+ T-lymphocytes is decreased and the remaining lymphocytes also have an alteration in function, resulting in progressive immune suppression, which will result in increased susceptibility to infections in those infected.

#### **1.3.2.2 Global burden**

In 2007, 33 million people were living with HIV, with 2.7 million new infections and 2 million deaths in that same year. Of these, 22 million were estimated to be living in Sub-Saharan Africa and 4.2 million in South and South-East Asia. Of the 7400 infections occurring every day, more than 96% are in low and middle income countries. Among infections occurring in the age group of 15 and older, 45% occur among young people (15-24), hence affecting largely the economically productive group (16). In the most affected countries, HIV has decreased life expectancy by more than 29 years, has aggravated household poverty and slowed economic growth (17).

#### **1.3.2.3 National burden**

In 2008, the adult HIV prevalence in Ethiopia was estimated to be 2.2%. The prevalence in that same period was estimated to be 1,037,267 among adults and 68,136 among children (18). Significant rural urban discrepancies remain with urban prevalence of 10.5% in 2006, according to the MOH (19). Unpublished data from the Addis-Abeba Health Bureau indicate that the prevalence of HIV was 7.2% in Addis-Abeba in 2008, with an all age prevalence of 156,577 and with 41,433 people in need for ART in 2008 (5).



### **1.3.3 TB/HIV co-infection**

#### **1.3.3.1. Pathogenesis**

The lifetime risk of developing TB from an infection with *Mycobacterium Tuberculosis* is 5-10% in an HIV negative person versus 50% in an HIV positive individual. The production of interferon gamma is decreased dramatically in parallel with the decrease in CD4+ T-lymphocytes associated with HIV infection. This leads to a significantly increased risk of developing reactivation or reinfection in HIV infected individuals. (11) HIV leads to progression to active TB both in people with recent and with latent infection. It is the most important factor in the reactivation of latent disease into active disease. It also increases the occurrence of recurrent TB, due to either reactivation or reinfection (20). HIV also leads to atypical presentations of TB as well as higher rates of smear negative and extra pulmonary TB (8,10).

Similarly, TB might also alter the course of HIV infection. Proinflammatory cytokine production by tuberculous granulomas has been associated with increased HIV viraemia, accelerating disease progression. The risk of death in a patient with HIV who has TB is twice that of an HIV patient without TB, adjusted for CD4 count, the death resulting not from TB but from HIV disease progression (11).

#### **1.3.3.2 Global burden**

Worldwide, about 11.1 million adults are estimated to be infected with TB and HIV. Seventy percent of these live in Sub-Saharan Africa, 20% in South East Asia and 4% in Latin America and the Caribbean (18). Over the past decade, some parts of Sub Saharan Africa have seen a 3-5 fold increase in the number of TB case notifications. It is also estimated that, in Sub Saharan Africa, one third or more of HIV infected may develop TB. In some areas of this region, rates of co-infection as high as 60%-70% have been reported (21).

#### **1.3.3.3 National burden**

In Ethiopia, data on TB/HIV co-infection is limited. Routine data from 44 sites in 2005/6 showed that the co-infection rate was 41% whereas another routine data in 2006/7

showed a rate of co-infection of 31 % (18). Hospital based studies have indicated rates of 50% and even higher (22). The WHO Global Report 2008 estimates that in Ethiopia, 40% of patients treated for TB are HIV positive (13).

#### **1.4. Global and national measures to control TB and TB/HIV**

##### **1.4.1. Global response to TB and TB/HIV**

In 1993, WHO declared TB a global emergency, a reflection of the magnitude of the problem. Different targets for TB control have also been set. In 1991, the World Health Assembly set a target to detect 70% of new smear positive cases in DOTS programmes and to successfully treat 85% of the detected cases, recognizing TB as a major global public health problem. The Millennium Development Goals (MDG) also set a target for TB control: MDG 6 Target 6C is to halt and reverse incidence by 2015. Two additional target impacts have been set by the Stop TB Partnership, which are to half prevalence and death rates by 2015 as compared to 1990 (15). Whether these goals are met depends on several factors. Different control strategies have been adopted to fight against TB and to meet the above mentioned targets.

One such strategy is the Directly Observed Treatment, Short Course (DOTS) strategy, launched by WHO in 1994. After further subsequent expansion and clarification, the framework has been implemented in 182 countries. Major progress in TB control has been achieved with the expansion of DOTS which has also helped national TB programmes, although the targets for TB control have not yet been met in every corner of the world. The five major components of this Strategy are:

- political commitment with increased and sustained financing
- case detection through quality assured bacteriology
- standardized treatment with supervision and patient support
- effective drug supply and management system
- monitoring and evaluation system and impact measurement

One of the most important components of the DOTS strategy is the direct observation of treatment (DOT), which implies that the patient should be supervised while taking

treatment, most often by a health worker. DOT's purpose is to ensure that patients take the correct treatment regularly (to achieve cure and prevent development of drug resistance); to find out quickly when a dose has been missed by a patient, in order to find out why that happened and to try and solve it; and to monitor any disease or treatment associated problem e.g. side effects. It is necessary to ensure that supervision is done in a patient sensitive and contextualized manner and that it is aimed to enhance adherence among both patients and providers. In addition, identifying physical, financial, social and cultural barriers to TB treatment is very important to ensure proper patient support (8, 13). DOT is surrounded by many controversies related to its effect compared to self supervision which we will come to in the literature review. The HIV epidemic has challenged DOTS as the sole strategy for TB control in Africa, because of the rising incidence of TB related to high HIV prevalence (23).

The Stop TB Strategy was launched in 2006 to achieve the 2015 impact targets and the targets for case detection and treatment success. It has six major components: DOTS expansion and enhancement; addressing TB/HIV, MDR-TB and other challenges; contributing to health system strengthening; engaging all care providers; empowering patients and communities; enabling and promoting research. In addressing TB/HIV, WHO's policy on TB/HIV collaborative activities is to be followed. This policy recommends twelve collaborative activities between TB and HIV/AIDS control programmes, classified in three broad categories:

- establishing the mechanisms for collaboration
- reducing the burden of TB in people living with HIV
- reducing the burden of HIV in people living with TB (8).

The need for TB/HIV collaboration is justified because the two diseases commonly occur together and impact each other; both TB and HIV patients will benefit from collaborative activities, and it would allow efficient use of resources, especially in view of the fact that health systems are overburdened by the high rates of TB infections related to HIV infections.

The Global Plan to Stop TB 2006-2015, fully adopts the Stop TB Strategy and its implementation is intended to bring various achievements in terms of expansion of equitable access for all of TB diagnosis and treatment; treatment and cure of millions of people; and sets forwards goals for introduction and improvement of drugs, vaccines and diagnostic tests (13).

#### **1.4.2. National response to TB and TB/HIV**

The recognition of TB as a major public health problem in Ethiopia dates to more than half a century ago. In the early 1960s, TB centers and sanatoriums were established in three major urban areas in the country, as an effort to control TB. In 1976, the Central Office (CO) of the National Tuberculosis Control Programme was established. In 1992, a standardized TB prevention and control programme, incorporating DOTS, was initiated as a pilot programme in Arsi and Bale zone, Oromia region. DOTS has been subsequently scaled up and implemented nationally, with a geographic coverage reaching 90%, whereas the Health Facility coverage is 75%. In June 2000, the previous Epidemiology / AIDS department of the MOH was restructured and named Disease Prevention and Control Department, and the TB and Leprosy Control Programme was incorporated into that department (13).

As any TB control programme, the general objectives of TB control programme in Ethiopia are to interrupt transmission of the infections; to reduce morbidity, mortality and disability; to prevent emergence and spread of drug resistance; to reduce the burden of TB among people living with HIV; to reduce HIV burden among TB patients, and the programme is aligned with the globally recommended Stop TB strategy and follows its strategies. The basic strategies in reaching the objectives are through early case detection, adequate chemotherapy, provision of comprehensive and standard patient care, enhanced case management, accurate monitoring and evaluation of programme performance and community participation. Community participation is intended to bring the health services as close as possible to the community, and to increase the demand and the awareness for the services. In addition, it can also enhance support to patients throughout treatment until cure, and it can also help in raising awareness about TB at patient, family

and community level. Community based DOTS introduced in the Oromia region in 2006, with Community DOTS supporters providing health education to the community, as well as tracing suspected patients and directly observing patients, has shown encouraging results with increased case detection rates although the effects on treatment outcomes were unknown. In addition, Public Private Mix (PPM) DOTS has also been started in 2006 as a pilot project in Addis-Ababa and Oromia involving for-profit health providers and is intended to improve the DOTS coverage and to increase case detection rates. The contribution of these private facilities is becoming apparent in that they already reported 1,266 cases (13).

The national response to the TB/HIV co-epidemics began in 2001, after WHO's call for implementation of TB/HIV collaborative activities for four countries in SSA including Ethiopia, which had high burdens of both TB and HIV. In 2002, a TB advisory committee was established. As part of expansion, TB/HIV collaborative activities are being implemented in 138 hospitals and 280 health centers and private clinics with ART services as of June 2007. Since then, key collaborative TB/HIV activities have taken place and have included: capacity building including training for regional TB and HIV/AIDS control programme managers and health workers; procurement and distribution of TB/HIV supplies; HIV testing of TB patients; provision of cotrimoxazole preventive therapy for HIV infected TB patients; referral to HIV related care, TB screening and referral among HIV infected patients; supportive supervision/mentoring and review meetings. In addition, Advocacy, Communication and Social Mobilization (ACSM) was advocated in order to create awareness about TB/HIV among the community in general and in those at risk in particular; in order to educate individuals, families and communities about transmission, prevention and treatment of TB and HIV; to ensure treatment adherence and to promote awareness about the dangers of defaulting treatment. Similarly, community involvement is also advocated, making both community based HIV and community based TB prevention activities work together (18). To what extent these strategies are being implemented and what their impact in the control of the dual epidemics is remains to be seen.

In addition, Ethiopia was among the first few African countries to introduce ART in selected health facilities in 2000, following the introduction of ART in resource-limited settings. The free ART service was launched in 2005(18). The ART program has been expanded since then to cover more regions and facilities (19).

### **1.5. Why is TB increasing globally?**

The question then is why, despite the many efforts that have been put both globally and nationally to combat TB both prior to and after the HIV epidemics and the increase in both international and national commitment to fight TB, it continues to be a major problem, and might continue to be so.

Many factors might play a role in the increase of TB worldwide. These include socio-demographic factors such as the increase in population worldwide, which occurs to a higher extent in populations where the prevalence of TB is already high; an increase in poverty worldwide, which results in overcrowding, under nutrition..., factors contributing to increased susceptibility and transmission of TB; and the HIV epidemic, again occurring mainly in areas already most affected by TB, and resulting in a significant increase in case rates (24). An increase in life expectancy, mainly in developed countries, also contributes to an increase in cases. The other problem is the emergence of multi drug resistant TB (MDR TB), and, according to WHO, 500 000 cases of MDR TB were reported worldwide in 2006, and, with the available laboratory and treatment facilities to date, countries project that they will only be able to treat 10% of the cases of MDR TB in 2008. In addition, shortage in funding also threatens to affect TB control with a funding shortfall of US\$1 billion for the 90 countries in which 91% of the world's TB cases occur, if they are to meet the 2008 Targets of the Global Plan to Stop TB (15). In addition, in less developed countries, two issues most common to the majority of locations are delayed presentation for treatment and defaulting from treatment, which threaten TB control programs (25).

All these factors also threaten the TB control in Ethiopia, a poor country with a rapidly increasing population; highly affected by the HIV epidemic and which is seeing an

increase in MDR TB; where diagnostic and treatment facilities remain poor and where donor funding is mandatory to sustain TB and TB/HIV programmes, especially in view of the increase in TB cases fuelled by the HIV epidemic. In addition, treatment delay and defaulting from treatment have also been described as problems that TB programs face in Ethiopia (26-33).

## **1.6. Adherence**

### **1.6.1. Definition**

Adherence is defined by WHO as “the extent to which a person’s behavior- taking medication, following a diet, and or executing lifestyle changes, corresponds with agreed recommendations from a health care provider” (34). It is important to note here the difference from the concept of compliance. In compliance, the guidelines given by physicians are assumed to be accurate and patient responses to treatment are measured according to these guidelines and hence it contains a value statement and a bias, allowing the issue of blame in the picture. As Farmer explains, the term also exaggerates patient agency, as it suggests that all patients possess the ability to comply- or refuse to comply- with anti-TB treatment, which he explains is far from true (35). According to Farmer, the poor are victims of “structural violence”, which includes factors such as poverty, racism, gender inequality...which affects them from the time of exposure to the disease all the way up to their access to health care (35). But the use of the concept of adherence is important in that it conveys a partnership between patient and physician. It also allows for a more comprehensive assessment of factors related to adherence such as characteristics of the regimen; attitudes of the providers; socio-economic, cultural and environmental factors (36). Therefore while addressing adherence we should not only address factors directly related to the patient but also the aforementioned factors, since, as Farmer notes, although adopting a patient centered approach is important, it is nevertheless insufficient: “The challenge to researchers is to acknowledge that adherence is influenced by a complex array of factors, many of which are beyond the patient’s control, and to begin identifying and describing these factors.”(35). The differentiation between the two terminologies is therefore of critical importance, although, in the literature, the two terms are sometimes used interchangeably.

### **1.6.2. Why study adherence?**

“Because the magnitude of non-adherence and the scope of its sequelae are so alarming, more health benefits worldwide would result from improving adherence to existing treatments than by developing new medical treatments.”

(WHO 2003)

Adherence to long term therapy for chronic illnesses in developed countries averages 50%, with rates possibly being lower in developing countries (34). The impacts of non-adherence are many, including poor treatment outcomes and increased health-related costs. Additional consequences, of public health importance, occur with infectious diseases such as TB. Non-adherence to TB treatment might lead to an increased risk of drug resistance and a prolonged infectiousness, in addition to relapse and death. This in turn will have implications not only for the patient but also for the community at large. Further discussion on this topic will be presented in the literature review.

### **1.6.3 How do we measure adherence?**

There are different ways of assessing adherence to treatment, and many methods are currently used. But there is no gold standard in the measurement of adherence (37, 38). One of the means of measurement of adherence is to ask patients and providers to subjectively rate their adherence or to use standardized patient administered questionnaires. This method might be liable to over or under estimation of adherence both from the side of the provider or the patient. The second method is the pill count, whereby remaining pills are counted when the patients come at treatment facilities, and with this strategy, in addition to counting inaccuracies, it is difficult to assess the timing of dosage and the patterns of missed dosages. A third approach is to do biochemical measurements in urine or blood of non toxic biological markers added to medications, but the results can be misleading and are liable to influence by factors such as diet, absorption and rate of excretion(34). Other methods such as assessment of pharmacy refills, electronic monitoring are also being employed and similarly display their own advantages and disadvantages.



In the case of TB, outcome oriented assessment of adherence is often made. The success of treatment, that is, the sum of the patients who are cured and those who have successfully completed treatment under the DOTS strategy being a proxy indicator of treatment adherence (34).

## **1.7. Literature review**

The literature on treatment outcomes/adherence to TB treatment is vast. Many studies, both quantitative and qualitative have explored the issue in different geographical contexts. But the study on adherence in TB/HIV co-infected patients, and in those on concomitant treatment, is scarce, as is the literature on the experiences of treatment and of illness perception in co-infected patients. The studies in co-infected patients and of those on concomitant treatment focus usually on the mortality of the patients studied. Some of those studies will be discussed because it is possible to make some assessment of adherence or because they reflect the problems that patients with co-infection on concomitant treatment face with regards to for e.g. complications of treatment. Thus, much of the literature review would be on patients with TB only, and I believe that many of the challenges or opportunities that patients with co-infection face with their TB treatment would be similar to those of patients without co-infection. I will begin with comprehensive reviews on TB/HIV and concomitant TB/HIV treatment and in addition discuss shortly about adherence to chronic treatment in general. In addition, a short review of the literature on adherence to HIV treatment will be made, since, in patients with co-infection receiving concomitant treatment, factors affecting adherence to ART could also potentially affect adherence to TB treatment. Review articles have been a large part of my literature review, since, as I mentioned above, the literature I'm exploring is vast and these articles provided a good summary.

In addition to review articles, I chose to discuss largely individual studies instead of grouping the findings into categories because I believed that it is important to see how different factors interact in a specific set up to affect adherence to treatment. Grouping findings into categories would overshadow the findings of studies, because, in most instances, multiple factors are associated with adherence in a specific study context.

### **1.7.1. Overview of co-infection and concomitant treatment**

I will start by discussing three review articles which provide an overview of the epidemiological and clinical aspects of co-infection. The pathophysiology and the burden of co-infection which are also discussed in these articles have been described above in the background section. In addition, these articles highlight the difficulties associated with concomitant treatment as well as the benefits associated with it. They point to the fact that concomitant HAART during TB treatment is complicated by high pill burden, overlapping drug toxicities, concerns about drug-drug interactions and paradoxical immune reconstitution reactions, and non-adherence to treatment. Because of this, there is an argument to delay or defer initiation of HAART during TB treatment. In addition, other barriers exist in the management of co-infection including the different ways in which TB and HIV are perceived, and their control systems set. In every case, the priority is to treat TB because of public health issues. The studies also discuss the effect of HAART on TB epidemiology. The case fatality rates of TB are 16-35% in patients not receiving HAART as compared to 4-9% in those who are HIV negative. The case fatality rates can be significantly decreased with the use of HAART as it shown by the example from England where mortality fell by 72% in TB patients with the introduction of HAART. There were mixed reports about discontinuation of treatment in patients on concomitant treatment. Drug toxicities were found to have led to discontinuation of either or both TB/HIV treatment in one study, and TB drug intolerance was also described in another study resulting in discontinuation of anti-TB treatment in 6% of patients. All three articles also discuss the Immune Reconstitution Inflammatory Syndrome (IRIS), most common in patients who start ART early in their TB treatment, and which presents as a worsening of TB signs and symptoms, and with frequencies of as high as 35-36% presented in some studies. The effects of IRIS on treatment adherence were not discussed. The optimal timing of ART during TB treatment is also discussed. That has been very difficult to determine because of the aforementioned factors. Experts' opinion on adherence when multiple medications are started at the same time is used in determining timing of ART in some guidelines, and not actual findings from studies, which are lacking. The studies also point that in Africa, TB is the leading cause of death among HIV infected patients; and often the first manifestation of HIV infection (11, 23, 39).

### **1.7.2. Medication regimen factors and their impact on adherence to chronic treatment**

A review of literature conducted in 2007 to assess the impact of medication regimen factors on adherence to chronic treatment, gave the following findings, although the authors underline the fact that it was difficult to get quality studies conducted within the area. The authors mention that several factors have been identified as correlates of adherence to long term medication regimens and include **patient factors** such as depression, health literacy, and substance use disorders, **environmental or contextual factors** such as social support and socioeconomic status, **clinician factors** such as clear communication and the time spent explaining the disease and treatment, **patient clinician relationship factors** like trust, **disease factors** such as chronicity, symptom prominence, response to treatment, **health care delivery factors** such as waiting time, pharmacy and clinic convenience, and **treatment regimen factors** such as pill burden, regimen complexity, side effects, duration of needed treatment and dosing schedule. In addition, the review showed that in most areas of chronic illness study, there is some evidence that greater dosing frequency is associated with poorer adherence. In some areas such as diabetes, hypertension, HIV/AIDS, strong and consistent evidence exists that dose frequency and regimen complexity are related to poorer adherence. The authors recommend that regimens as simple as possible requiring the fewest doses per day would help improve adherence (40).

Similarly, a review of studies which used electronic monitoring to measure adherence published in 2001 also showed that the higher the number of doses prescribed per day, the lower the adherence, with less frequent dosing resulting in better compliance for a variety of therapies(41).

Another review article published in 2003 to see the health outcomes and health care costs of reduced dose frequency also supports the above findings with reductions in daily doses resulting in improvements in adherence. Advantages associated with fewer doses per day included the avoidance of social stigma of taking medications in public, the feeling of being less dependent on medications, the reduced chance of taking duplicate medications, and the convenience of the dosing schedule (42).

### **1.7.3. Studies in patients with co-infection**

A study conducted in Portugal to assess determinants of an unfavorable TB treatment outcome (no cure or death) and to assess determinants of non-adherence in HIV positive TB patients on ART, showed that 32.9% of patients were non-adherent to treatment and that 22.9% had an unfavorable outcome. Non-adherence was found to be the only predictor of an unfavorable outcome and adherence was independently associated with I.V. drug use, treatment complications and use of methadone. In this study, the sample size was small (70 patients), and the timing of ART initiation was not mentioned (43).

A retrospective cohort study conducted in England to assess the risks and benefits of administering HAART during the treatment of TB in HIV infected patients showed that there was a significant decrease in viral load and AIDS defining illness in those who were initiated on ART, as well as a decrease in mortality. In addition, there was a significant association between the occurrences of adverse events and use of ART. 10% of patients had paradoxical worsening, 90% of whom were on ART. The authors point out the fact that the occurrence of AE could potentially influence adherence to either disease but there was no evidence of it in the study (44).

A study conducted in Malawi to assess whether ART reduces case fatality among HIV-positive patients with TB, in which patients who received ART in the continuation phase of TB treatment were compared to those who didn't receive ART showed that ART started in the continuation phase didn't have any effect in reducing case fatality (6 out of ten deaths occur in the intensive phase). Similarly, the other treatment outcomes were also similar in the two groups e.g. treatment success, loss to follow up...although that was not discussed by the authors. The limitation in this study is that the two groups compared were patients who accepted and those who refused ART, hence there might be differences in economic or social status between the groups which influenced treatment outcome (45).

Another study was also conducted in Malawi to compare 6-month and 12-month cohort treatment outcomes of HIV positive TB patients and HIV positive non TB patients treated with ART, and this study showed that those patients with TB had a significantly

lower default rate and the authors discussed that it was possibly due to the fact that these patients had time to stabilize and prepare for their ART since they were started on ART only in the continuation phase of TB treatment, whereas the other patients were started on ART in a short time (46). Thus, this can indicate that adherence to either treatment (anti-TB or ART) might be a challenge for those patients who start the ART drugs in the intensive phase of anti-TB treatment.

A study conducted in Nigeria to compare the treatment outcomes of TB/HIV positive and TB/HIV negative patients showed that default rate, which was 17% overall was not significantly related to HIV status, although more HIV positive than HIV negative patients defaulted from treatment. It was also found that reasons for default to TB treatment in the HIV positive patients included: severely ill patients going back their home town to receive support from their extended families; patients leaving the area to consult healers that advertised that they would cure HIV; seriously ill patients not being able to come to collect their drugs personally; stigma and discrimination forcing some HIV positive patients to relocate, mainly those with HIV wasting and other obvious HIV related symptoms. The study showed a significant difference in mortality (15.5% in HIV positives VS 3.1% in HIV negatives.) The HIV positive patients were not on ART in this study (47).

Two studies conducted in England also showed that paradoxical reactions during TB treatment were more common in co-infected patients receiving ART, mainly when introduced early (48); adverse events also occurred more frequently in HIV positive patients in one study comparing HIV negative patients with HIV positive patients (of whom 70% received ART). But despite a greater rate of serious adverse events such as hepatotoxicity, peripheral neuropathy, rash, persistent vomiting, in the HIV positive individuals, TB treatment discontinuation was similar in the two groups (49).

Two studies on adherence to TB preventive therapy in HIV positive patients showed high rates of default. 26.5% of patients defaulted from preventive treatment in Thailand, with migration for job search, denial of HIV status, perceived drug side effects, and

confusion about the duration of treatment being associated with defaulting. Married people, women, outpatients, surviving spouses, the self-employed, and those with no history of physical symptoms were more likely to be adherent to the treatment (50).

Similarly in South Africa, more than half of HIV patients initiated on TB preventive treatment interrupted it, with fear of stigmatization, lack of money for food and transport, the belief that TB is incurable, competition between western and traditional medicine, and reluctance to take medications in the absence of symptoms being barriers to adherence and disclosure of HIV status, social and family support, a supportive clinic environment positively influencing adherence (51).

#### **1.7.4. Studies on adherence to TB treatment and on perceptions about TB and its treatment**

Hereunder, I will present selected articles on adherence to TB treatment in different settings and studies which focused on understanding/perception about TB.

First, I will discuss a recent systematic review of qualitative research on adherence to TB treatment. The aim of the review was to understand factors considered as important by patients, caregivers and health care providers for TB medication adherence. Eight major themes came out; **organization of treatment and care for TB patients**, with factors such as distance from institutions, availability of transport, long waiting times, inconvenient appointment times, maltreatment by providers, rigidity of DOT... affecting adherence; **interpretation of illness and wellness** with patients discontinuing treatment once they felt well, others continuing treatment because they felt encouraged by improvement, others discontinuing treatment when they saw no improvement in their condition...; **financial burden of TB treatment** with loss of job associated with TB diagnosis, difficulty to obtain sick leave, difficult choice between the need to attend clinics or earn a living, excessive costs of treatment...affecting adherence; **knowledge, attitudes and beliefs about TB treatment** with understanding about the treatment, its duration, beliefs in treatment efficacy, fear and denial of diagnosis... affecting adherence. **Law and immigration** with legal and immigration requirements in certain set ups influencing patients' adherence; **Personal characteristics and adherence behavior** with substance abuse, mental illness, particular ethnic groups, age, sex, religion, literacy...

affecting adherence; **Side effects and adherence** with side effects resulting in discontinuation of treatment and at times being given cultural meanings by patients; **family, community and household influence** with the strong influence of stigma on adherence, and the contribution of family support be it financial, emotional influencing treatment. The study also indicates a lack of evidence on the experiences of patients living with HIV/AIDS and taking treatment for TB or for both illnesses (52).

Another recent review of qualitative research which reported on experiences and perception of TB and its treatment of people with or at risk of TB, health service providers, policymakers, also came up across similar themes which were classified into five themes: **Socio-economic circumstances, material resources and individual agency:** poverty and disadvantage played a negative role in the delay as well as in the treatment of patients (and some groups such as drug and alcohol users, refugees and migrants were particularly vulnerable in some set ups). This through an inability to give up work or risk losing their income though attending treatment; and dealing with costs including transportation costs, drug costs and costs related to food. In many instances, patient struggled to overcome these barriers as far as their finances and other circumstances allow. **Explanatory models and knowledge systems in relation to TB and its treatment:** diverse patient beliefs about TB and its treatment were found to shape their decisions regarding treatment. For example, patients who believed that TB is a punishment from god were found to revert to non medical healers. **The experience of stigma and public discourses around TB:** across many cultures, widespread TB related stigma exists, articulated by public discourses around TB, resulting in people being reluctant to seek diagnosis or to be seen taking treatment and studies focusing on gender indicate that women suffer from stigma more than men. **Sanctions, incentives and support:** punitive sanctions such as threats of deportation, imprisonment were adversely affecting treatment while incentives such as provision of food and transport money and detoxification programs were found to be positively influencing adherence. Financial and social support from families and friends were also found to be of critical importance for adherence. **The social organization and social relationships of care:** services were found to be rarely designed taking the patients' needs into consideration. Inconvenient

treatment schedules, distance to health facilities, as well as inpatient management were found to be difficult for patients. In addition, lack of health education, poor quality services mainly in governmental centers, and poor relationship between providers and patients, as well as misunderstanding and miscommunication between patients and health providers were found to adversely affect adherence (53).

Individual studies from different countries that I reviewed were in line with the findings of the two above review articles. Different factors were found to play a role with regard to adherence in many settings. Findings from selected studies are discussed below.

A case control study from Nepal showed that longer travel to health facility, not being informed about the consequences of defaulting by health professionals, side effects such as vomiting, stomach problems and itching which patients were not informed about, health care workers' behavior, health service failure were associated with defaulting whereas desire for cure and knowledge that TB is curable were most important for completing treatment among those who successfully completed treatment (54).

A case control conducted in Madagascar showed that long transportation time, male sex, poor information given to the patient by health professionals, poor communication between patients and health providers were significantly associated with default. Males were thought to default more than females because they have to reconcile work with treatment, males having paid work more frequently than females (55).

In Uganda, a retrospective cohort study showed that treating patients at one unit, treating patients near their homes, training and supervision of health workers and progressive use of short course chemotherapy were associated with high treatment completion, with significant increase in the rates of treatment completion in the set up; with a default rate of 8.8% among survivors (56).

In Malaysia, a default rate of 28.8% was found in a prospective cohort study which showed that patients had misconceptions about TB and its treatment, with many getting



the information from friends or relatives. Patients who thought about disappearance of symptoms as cure tended to have a higher default. Patient characteristics such as age, sex, education did not affect adherence (57).

In a cross sectional study conducted in Zambia, a default rate of 29.8% was found, and it was also found that beginning to feel better, lack of knowledge on the benefits of completing a course, running out of drugs at home, TB drugs being too strong were associated with non compliance, whereas there was no association between age, marital status, educational level and compliance (58).

In Nigeria, a default rate of 23% was found in a retrospective study. The study showed that the important risk factor associated with compliance was male sex, which was explained by the authors as resulting from the fact that males were usually the breadwinners in the society, and had difficulty to comply with treatment, mainly the daily attendances at the clinics. Defaulting was highest in the continuation phase of treatment, with 78% of defaults occurring in the continuation phase with HIV positive patients having twice the risk of default during the intensive phase as HIV negative patients. HIV status was not associated with defaulting (59).

In the United States, two studies showed that increasing incentives is related with higher treatment adherence in different population groups where increase of preexisting incentives at treatment centers resulted in improved adherence to TB treatment (60) and to prophylactic treatment among intravenous drug users (61). Previous TB, resistance to rifampicin, human immunodeficiency virus infection, psychiatric illness, homelessness, smoking and drug use were related to non-adherence in the first study. A review of 11 randomized controlled trials on the effects of financial incentives (cash, vouchers, lottery tickets, or gifts) on compliance to different treatments has similarly shown that incentives increased compliance in 10 of the 11 trials, with all trials being conducted in the United States (62).

In Ghana, a default rate of 13.9% was found in a study combining focus groups with cross sectional survey which showed that a good relationship between patients and health staff was the main facilitator of adherence while financial difficulty was the main barrier to adherence. Monthly income, lack of social support and problems relating with others while on treatment were also significantly associated with default. Stigma attached to TB made patients deny diagnosis or hide their illness (63).

In Burkina Faso, a qualitative study (observation, FGDs, in-depth interviews) showed that patients resort to traditional healers or self treatment before seeking medical help because of financial and cultural reasons; those starting anti-TB treatment faced problems to get to the health services (long distance, poor transportation, expenses related to transportation) and problems while at the health services (health provider attitude, waiting time) (64).

In Pakistan, a focus group study showed that TB was perceived as a dangerous and incurable illness, which leads to stigmatization and social isolation of TB patients as well as their families; the problems being worse for females, who risked divorce and low chance of marriage. Patients often deny diagnosis or refuse treatment because of fear of the negative impacts of having TB. Pregnancy was also found to be a reason for stopping treatment. Patients were found to face diverse socio-economical problems, worse on women because of their economic dependence on males (65).

In India, a qualitative study (in-depth interviews, observation) showed that convenient clinic timings, arrangements for the provision for treatment in the event of a family emergency and provision for complicated cases like alcoholics were needs of patients that were not met by the health system. Lack of attention and support at the clinic, long distance to the clinic, difficulty of reentering system after missing treatment because of labeling by health professionals, equating well being with cure also affected treatment (66).

In South Africa, a qualitative study (interviews, FGDs) showed that there were misconceptions about the origin of TB and its treatment. TB was thought by 60% of patients to result from the breaking of cultural rules and that it can only be treated by traditional healers. TB was also thought to be due to mine work, malnutrition, infected food, smoking, alcohol and sexual contact. The stigma of TB (due to the fact that people with TB were thought to have broken cultural rules as well as its association with heavy drinking and poverty), the belief that there should be abstinence from sex while on treatment, difficulties to access health services, long waiting time and health worker attitudes were found to influence adherence to treatment (67).

In Kenya, a qualitative study (FGDs) showed that TB is perceived as a contagious disease difficult to treat. TB treatment is perceived as long, agonizing and rough. Misperceptions exist as to its origin i.e. alcohol, smoking, exposure to cold, hard work, hereditary. Prolonged self treatment until symptoms become severe, alternative treatment (traditional), the stigma associated with the disease (with patients and their families being isolated by the community) lead to treatment delay and these factors can also influence adherence (68).

A recent systematic review on the timing of default from TB treatment showed that, in the 15 studies included, many patients default in the later stages of treatment, with majority of patients completing the intensive phase of treatment (69).

A review of interventions to promote adherence to TB treatment showed that, in the 14 trials included, reminder cards sent to defaulters, a combination package of a monetary incentive and health education and more supervision of clinic staff increased the number of people completing their tuberculosis treatment. One trial showed that intensive counseling/education did not help improve adherence. DOT was associated with better outcomes in one study, showed no difference in another study (70).

A review of trials comparing DOT with self supervision of treatment conducted in low, middle and high income countries showed that there was no difference in cure or

treatment completion in the two groups. Similarly, there was no difference in cure or treatment completion between patients supervised by different people (health professional, lay health worker, family/community member) (71).

In Thailand, a focus group study conducted to see the effect of high AIDS awareness on TB management showed that there were many misperceptions about TB transmission; the participants had a better awareness about HIV as compared to TB. Both illnesses were stigmatized, although more stigma was attached to HIV. Symptoms of TB were perceived as being symptoms of HIV, leading to people being suspected of having HIV when they had TB. This led to delay in seeking treatment and non-adherence to TB treatment in patients who suspected they had HIV and feared for it to be detected (72).

#### **1.7.5. Adherence to ART**

A review of literature on adherence to HAART regimen indicated that barriers of adherence to ART treatment are similar to barriers to chronic treatment in general: **regimen complexity**, with pill burden but mainly dosing schedules and food restrictions affecting adherence, but regimen that best fits the daily schedules and patients' attitude towards treatment being stronger predictors than dosing schedules; **side effects** resulting in poor tolerability (with transient or long lasting side effects at times resulting in treatment discontinuation), studies showed that adherence is optimal when symptoms are controlled and declines with the occurrence of side effects; **patient related factors** such as forgetfulness which happens mainly when symptoms have improved, and difficulty in understanding treatment schedules; **psychosocial issues** such as depression, stress, hopelessness, substance abuse adversely affecting adherence whereas support from families, friends, treatment buddies and peer counseling were found to facilitate adherence; **patient belief system** with greater adherence found in those who believe that HAART is effective, and **patient provider relationship**, with the pivotal role of adherence counseling. A good patient provider relationship assists adherence whereas miscommunications and unmanaged side effects frustrate patients and lead to non adherence(73).

A study conducted in Uganda, Tanzania and Botswana and which used qualitative methods to identify context specific constraints to adherence showed that, despite a high motivation on the side of the patients to take drugs, some factors were challenging adherence. These included transport costs and user fees, and at times absence of adequate transportation; waiting times averaging as high as 5 hours in some set ups with patients having to miss their daily work for their drug refills; hunger, mainly when the body regains strength and weight, was a common problem for patients with some discontinuing treatment because of lack of food; HIV related stigma was found in all the countries, with loss of job, isolation by families and community members reported, and many patients chose not to tell about their HIV status to families, hence having to hide their medication intake which resulted at times in irregular intakes, but also patients resulted in patients not being able to get social support; side effects had lead to treatment discontinuation in patients, and patients in Tanzania and Uganda were not informed about side effects and that these could subside over time but patients in Botswana were given extensive information about side effects in pre-treatment counseling and few mentioned side effects as a reason for treatment discontinuation. The quality of counseling, which is a key requirement for successful ARV adherence, was found to be variable in different countries as well as within different parts of the same country, and patients in Uganda valued the support of community based volunteers who were HIV positive themselves. Heavy workloads at the clinics were also challenges noted in the three countries, since ART scale up was not followed by an increases in health personnel, but despite this workload, an absolute majority of patients reported being satisfied with the services provided at the health clinics (74).

#### **1.7.6. The literature from Ethiopia**

In Ethiopia, few studies have explored knowledge/perceptions about TB. Adherence to TB treatment has been studied better. Most of the studies conducted are quantitative studies. I will discuss each study below. In addition, I will discuss two articles on treatment delay, since factors affecting treatment delay might similarly affect adherence and I will also discuss one article on acceptability of HIV counseling and testing and three articles on ART treatment adherence.

In 1989/90, a cross-sectional study was conducted in Addis-Abeba, consisting of 1206 new TB patients with the aim of identifying the rate of defaulting from treatment and factors associated with it. A default rate of 82% was found, with rates of defaulting being higher in males, in the older age group and in those living near to the TB center. Most of the defaulting occurred in the third and fourth month, with feeling of improvement and social problems as the two top reasons for defaulting. In addition, comparison of defaulters and a control group of non-defaulters showed that inadequate knowledge, low educational level, nearer distance to the health center and negative attitude towards the TB center were significantly associated with defaulting (75).

An institution based cross sectional survey was conducted in 1996, in a rural health center in the South Gondar region with interview and respective review of medical records of 211 TB patients. It showed that social ostracism had affected TB patients and their families to a great extent, with patients and healthy family members excluded from social and religious ceremonies for fear of contagion. A divorce rate of 29.1% due to TB was reported. In addition, patients reported loss or threats to lose their job. Dietary misconceptions were also found to be very common, with patients avoiding millet, maize, sorghum, potatoes and onions fearing that these will decrease the potency of anti-TB drugs. Many patients similarly avoided sex during treatment since they thought that it will decrease the potency of the drug, which in turn impacted on their marriage. The study also showed that control activities were ineffective and poorly organized (76).

A community based cross sectional study was conducted in 1997 in the Northwest region to assess the perspective of the rural community towards TB and TB patients. 1000 heads of household were interviewed and information about the disease obtained for 5078 family members. TB treatment defaulters were found in 10% of the households, with apparent clinical improvement after the intensive phase being the reason for defaulting in 45% of the cases and far distance to the health institution contributing for 25.3% of the reason for defaulting. Evil spirit, contaminated food/water and sexual intercourse were thought to be causes for TB in 19.9%, 18.6% and 4.7% of respondents. It was also found that the community exhibited high ostracism towards TB patients, with a majority of

respondents not allowing attending social gatherings or festivities with a TB patient on treatment. With 76.2% of respondents having heard about HIV/AIDS, 19.4% also said that there could be an association between HIV/AIDS and TB (77).

Another cross sectional study was also conducted in the same year in the Harar region, and it included 418 pulmonary TB patients. In this study, comparison between HIV positive and HIV negative patients showed that HIV positive patients were more defaulters than the HIV negatives, although not significantly. In addition, that study showed that HIV positive patients had significantly higher levels of secondary drug resistance and that significantly higher numbers of them were cases of relapse and treatment failure (78).

In 1999, a case control study was conducted in the Oromia region, in which the records of 1367 patients were reviewed to determine the defaulting rate. A default rate of 11.3% was found. Defaulting was highest (81%) during the continuation phase of treatment. Comparison of cases (defaulters) and controls showed that medication side effects were significantly associated with defaulting while adequate knowledge and family support were protective against defaulting (29).

A cross-sectional study was conducted in 1999/2000 in the Jimma area among patients in the DOTS regimen to determine the rate of defaulting and associated factors. It showed an overall rate of defaulting of 6.7%. 52% of the defaulters were traced and their reasons for defaulting were sought. The major factors contributing for defaulting were socioeconomic factors including distance of patients' residence from the health institution, lack of money for paying transportation and poor awareness about the disease (30).

A prospective cohort study was conducted in 2002-2004 in Southern Ethiopia with the aim of determining factors predicting treatment adherence in smear positive TB patients. It showed a default rate of 20% among the 404 patients involved. Most treatment interruptions (91%) occurred in the continuation phase of treatment. Again, distance from

home to treatment center was related to defaulting; as well as the necessity to use public transport to get to a treatment center and age>25 years (28).

Two studies have also been conducted to assess the effects of TB clubs on TB control. The first, a descriptive study conducted in the South Gonder region to assess the impact of “TB clubs” on the performance of the TB programme, showed that the introduction of the TB clubs helped to significantly increase the proportion of actual among expected attendances of tuberculosis patients for follow-up during treatment at health facilities. TB clubs together with other community members, also referred TB patients, promoted adherence and traced defaulters. TB clubs were also involved in the identification of the majority of new smear positive patients (79).

The effectiveness of TB clubs in improving compliance to TB treatment and in improving societal attitudes towards TB was also assessed by another study conducted in Northern Ethiopia. The study utilized a combination of a cohort study with focus groups and in-depth interview. A significantly higher treatment completion rate and a significantly lower default rate were found in the TB club group as compared to the comparison group. The qualitative study showed significant changes in patients’ understanding of TB, their reaction to initial diagnosis, misconceptions as to the cause and treatment of TB, the social isolation and compliance and belief in the modern health care in the TB club area (80).

A qualitative study consisting of in-depth interviews and focus groups was conducted in 2001/2002 in Addis-Abeba to explore how symptoms of TB are perceived and managed from the onset of symptoms and during the course of treatment. It showed that TB was largely thought to be due to exposure to “bird” (cold), misperceptions existing even among health professionals. Early symptoms of TB were treated at home or in private clinics where patients were usually offered antibiotics to rule out pneumonia, resulting in treatment delay. Some patients related TB to supernatural forces; and many patients thought that TB could restart, leading to a non-curable type of TB, chronic type of TB or AIDS. AIDS was perceived as a second stage of TB. For many patients, cure would



necessitate proteinaceous foods in addition to the drugs, in addition to avoiding actions such as sex. It was also found that adequate information about the treatment was not provided to the patients by health professionals (81).

The same authors explored enablers and barriers in the management of TB treatment during the first five months of TB treatment in Addis-Abeba, and showed that many socio-economic factors affected patients' adherence to treatment. These included loss of employment and the possibility to work, the difficulties associated with daily treatment and rigid routines existing in the health clinics, and financial problems faced by patients. In addition, the financial and practical help that patients received from relatives or communities would be lost over time, making them vulnerable to default in the later stages of treatment. Those mainly affected being those who were unable to regain their health early. In addition, the researchers noted that there was a strong association between TB and HIV/AIDS and that if the patient had a "curable disease", he is expected to show improvement within a certain period of time and if that does not happen, he would be labeled as someone having an incurable disease (AIDS or a chronic type of TB), leading to additional stigma (31).

Two studies were also conducted to assess the effect of DOTS on treatment outcomes of TB patients. The first study, a register based analysis of 19971 patients registered between 1994 and 2001 in the Southern region of Hadiya, showed that, with a population coverage of DOTS reaching 75% in 2001 and 94% of patients being treated with short course chemotherapy, treatment success increased from 38% to 73% in 2000 in smear positives; default rate declined from 38% to 18%. Being a female patient, age 15-24, smear positive pulmonary TB, treatment with short course chemotherapy, treatment at peripheral centers were associated with higher treatment success and lower default rates (32).

The second study explored the treatment outcomes of 136,572 patients treated between 1995 and 2004 in the Southern region, and it was found that the decentralization of DOTS had significantly improved treatment outcomes with significant improvements in

the case detection rate, the case notification rate and the treatment success rate. The default rate decreased from 26% to 6% in that period (33).

Inadequate knowledge about TB and distance from home to health centers were found to be associated with delay before diagnosis, in a cross sectional study conducted in 1998 in Addis-Abeba, which included 700 TB patients, and which showed a high delay (26). Another cross sectional study conducted in 2004 in the Amhara region, which included 384 new smear positive patients, also showed an increased delay (both patient and provider), with a median total delay of 80 days. It also showed that self treatment and visit to non formal health providers were strongly associated with patients' delays (27).

Three studies on adherence to ART treatment were also reviewed. The first, a recent cross-sectional study combined with in-depth interviews, conducted in Addis-Abeba among 431 HIV patients, showed a self reported adherence rate of 81.2%. Being too busy or simply forgot and being away from home were the major reasons for non-adherence whereas not being depressed, having no side effects, a regimen that fitted the daily routine and satisfaction with the relationship with doctors were found to be facilitators of adherence. Financial problems, medication side effects, lack of knowledge about the need for adherence emerged as major barriers in the interviews; and social support was reported as a facilitator of adherence (82).

A case control study conducted in the same region also showed that 13.6% of patients who had not come to the clinic had defaulted. Less than 40% of defaulters were traced because of incorrect address but, among those who were traced, loss of hope in medication, lack of food, mental illness, holy water, no money for transport, and other illnesses were given as reasons for defaulting. In addition, taking hard drugs (cocaine, cannabis and IV drugs), excessive alcohol consumption, being bedridden, living outside Jimma town and having an HIV negative or unknown HIV status partner were associated with defaulting ART (83).

In addition, a cross sectional study conducted in Arba Minch Hospital in 2005 and which included 190 TB patients showed that women were more likely to be infected and that the acceptability rate of HIV testing was only 35%. Being unemployed was found to be the only factor associated with accepting the test (84). The implications of this study are that it might be difficult to scale up TB/HIV collaborative activities with such a low acceptability of HIV testing and that the reasons behind such a low acceptability of testing might also affect adherence to treatment in co-infected patients.

### **1.7.7. Summary of the review and gaps identified**

The literature review shows that adherence to TB treatment has been studied across different settings. It shows that non adherence to TB treatment remains a problem in different parts of the world, although the magnitudes differ. Many factors seem to influence TB treatment adherence similarly in many settings. The studies on co-infection showed mixed results as to the impact of HIV infection on adherence to TB treatment, with some studies indicating an association between HIV status and TB treatment adherence and others showing no relationship. From the different studies reviewed, it is possible to see that personal characteristics such as age, marital status are unstable predictors of adherence, whereas other factors such as costs related to treatment, distance to health institution, patient-provider relationships... seem to have a uniform effect on adherence across studies. Needless to say that some of the barriers and facilitators of adherence are very much context specific for example reflecting specific illness perceptions in communities. In many instances, several factors are associated with non adherence to treatment in patients.

Studies exploring beliefs/attitudes about TB and its treatment are very important in understanding patterns of adherence in a community, but such studies are lacking compared to studies on adherence.

Similarly, despite the high rates of co-infection globally and in particular in Sub-Saharan Africa, and despite fear of poor adherence in patients on concomitant treatment

among the medical community, few studies have focused on this subject, rather, the focus in co-infected patients has been to see prognosis and how prognosis is affected by the provision of ART to TB patients.

The studies from Ethiopia, largely quantitative and conducted mostly in rural areas have also identified socio-economic and structural barriers to adherence, and have also indicated that high TB related stigma exists within communities. Adherence rates in general seem to have shown improvement over the past decades (from 82% in 1989 to rates as low as 6.1% in recent years). In addition, a study conducted in Addis-Abeba in 2001/2 indicates that there is a strong association between TB and HIV/AIDS and that AIDS is perceived as a second stage of TB which is thought to be incurable. This needs to be explored further and how these misperceptions and other factors act as barriers and facilitators of adherence to TB treatment in co-infected patients need to be studied. In addition, although the quantitative studies point to factors that can potentially affect adherence, they fail to show us how these factors actually interact to lead the patient to make a decision regarding his/her treatment and this is better explored through a qualitative approach, but qualitative studies are very few in Ethiopia.

## **1.8. Objectives of the study**

### **1.8.1. Overall objective**

- To provide knowledge for improvement of tuberculosis treatment outcomes in patients with TB/HIV co-infection receiving concomitant treatment

### **1.8.2. Specific objectives**

- To describe general clinical characteristics of tuberculosis in co-infected patients who received concomitant ART treatment
- To describe magnitude of default and factors predicting tuberculosis treatment adherence in these patients
- To compare TB treatment outcomes with a comparative group of HIV negative patients

- To explore co-infected patients' perspectives of facilitators and barriers to tuberculosis treatment adherence
- To explore health workers' perspectives of facilitators and barriers to tuberculosis treatment adherence

## **1.9. Justification for the study**

Ethiopia is one of the twenty two high burden countries for tuberculosis. The rate of TB/HIV co-infection is also high (30%-50%).

Concomitant treatment in co-infected patients is complicated by factors such as high pill burden, overlapping side effects, drug interactions, double stigma (TB and HIV related). How these factors affect adherence to TB treatment in co-infected patients on concomitant treatment together with other factors (socio-economic, structural...) has not been well studied, although expert opinions point to the fact that concomitant treatment might adversely affect treatment adherence, especially when ART is initiated in the intensive phase of TB treatment.

As to my knowledge, understanding of co-infection and how it impacts on adherence to TB treatment, and the experience of concomitant drug intake, as well as the effect of double stigma on adherence to anti-TB treatment among other things have not been explored in Ethiopia and I would like to explore this gap.

## **Chapter two: Subjects, materials and methods**

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### **2.1. Study area**

The study was conducted in Addis-Abeba, in three health centers randomly chosen among 21 health centers. These health centers are administered by the Addis-Abeba Health Bureau and provide general medical services for the populations within their catchments areas. The health centers randomly selected were Bole Health Center, Arada Health Center and Woreda 7 Health Center. Although the TB clinics have been operating for many years in these health centers, the ART clinics have started working since 2006 as part of the expansion of HAART provision program initially started in hospitals. The health centers offer free ART service and chronic HIV care for patients with HIV infection. In addition to diagnosis and treatment of patients with TB, the TB clinics located in these Health Centers also offer the Provider Induced Counseling and Treatment (PICT) service through which all patients coming to the TB clinics are offered screening for HIV. Both TB and ART treatment are offered for free in the health centers and the following regimens are used.

1. Regimens used for the treatment of TB: according to the guidelines of the National Tuberculosis and Leprosy control program, all new cases of TB are treated with short course chemotherapy, which is constituted of two months on RHZE (rifampicin, isoniazid, pyrazinamide, ethambutol), followed by a continuation phase of six months on EH. During the intensive phase, patients are supervised by health workers daily while taking treatment. In the continuation phase, drugs are self administered and collected on a monthly basis. Patients who are on retreatment because of default, relapse or treatment failure are treated with RHZE plus streptomycin (S) for two months, followed by one month treatment with RHZE, and five months treatment with RHE. Retreatment cases are to be supervised throughout treatment. Dosage is dependent on weight of the patient. Fixed dose combinations are used throughout.

2. ART regimens used: the following HAART regimens are available in the health centers:

- Stavudine/lamivudine/nevirapine
- Stavudine/lamivudine/efavirenz
- Combivir/Nevirapine

- Combivir/Efavirenz

Fixed dose combinations (FDC) have recently been introduced in the health centers. Patients in our study have not used these FDCs during concomitant therapy. In addition, second line regimens are also being used, but in hospitals only.

When to initiate ART in the treatment of TB patients co-infected with HIV remains a controversy. In Ethiopia, the national recommendation is to start patients with CD4 of < 50 on ART as early as possible; for those with CD4 between 50 and 200, initiation of ART should be within 2-8 weeks after anti-TB initiation and for those with CD4 > 200 (200-350), ART is to be initiated once the intensive phase of anti-TB is completed.

The different health centers in general do not have significant differences in terms of services they provide and in terms of health personnel and equipments available.

My initial plan was to conduct my studies in Hospitals providing ART services, since they were the ones where free ART treatment was first started in 2005. In addition, patients diagnosed in these hospitals were sent to nearby TB clinics for their TB treatment, so I wanted to explore the difficulties for patients of attending two treatment centers. But, when I got to Addis-Abeba and visited some hospitals, I found out that the TB treatment outcomes were not recorded for many patients at the ART clinics, and that it would be very difficult to trace the patients for whom the outcomes were unknown back to the health centers because the exact health center they were referred to was unknown in most of the cases. So, I decided to conduct my study in the health centers where both TB and ART services are provided.

## **2.2. Study design**

The study adopted a combination of methods, quantitative and qualitative. The quantitative component was a register based retrospective cohort analysis of TB/HIV co-infected patients aged 16 years and above registered for tuberculosis treatment in the period July 2006-August 2007 and who had been on ART treatment while on TB

treatment, irrespective of the timing of ART initiation in the course of TB treatment. We reviewed both the TB treatment registers and the HIV clinic charts of the patients to record information we wanted. We similarly collected the TB treatment outcomes of HIV negative TB patients, starting from the beginning of our inclusion period going onwards until we reached a similar sample size as the HIV positive patients, including all consecutive HIV negative patients, to minimize possible selection bias. This group was included in order to describe differences in treatment outcomes between the two groups. TB clinic registers were reviewed for the HIV negative patients.

Retrospective studies are cheap and non time consuming. But important information might be missing or otherwise unavailable while conducting retrospective studies (85). In my case, this was the study of choice, because, even though conducting a prospective study allows for careful control of the nature and quality of data recording (86), in my case allowing the recording of factors which could potentially affect adherence at the beginning of the study; it would nevertheless be impossible to conduct such a study within the time frame allocated for field work (six months).

The qualitative component consisted of in-depth interviews with purposefully selected patients and health professionals and focus group discussions with purposefully selected patients. In-depth interview is one form of qualitative interview. It is important in dealing with issues which involve private matters such as adherence, and is good to explore issues which involve complex phenomena. It allows us to see how the meaning making process unfolds in the interview, in addition to giving an answer to what is enquired. It allows us to see the interrelatedness of the whats and hows (87). Focus groups can be used to get an early impression of a target population, to develop interview guides, to validate and elaborate information gathered by other means (88). They are advantageous in that it is possible to involve 6-12 participants at the same time. The disadvantages are the difficulty to choose homogeneous groups, and the fact that it might be difficult to discuss personal and sensitive issues in groups (89).



Mixed methods approach (combining qualitative and quantitative methods) can be used to either meet different needs at different stages of a project, to compensate for shortcomings of either method or for the purpose of triangulation. Triangulation involves the gaining of multiple perspectives through combining completed studies conducted on the same topic and that directly address each other's findings. One method should either challenge (or clarify), illuminate (or add to the other) or verify (provide same conclusion to) the other. When used for triangulation, the methods are used either sequentially or in parallel. In this case, each study is conducted independently and is complete by itself and the results inform each other (90). In my case, I combined the methods for the purpose of triangulation. I wanted to see the clinical characteristics, treatment outcomes (in particular default vs successful treatment) and associated factors in patients with co-infection on concomitant treatment, and I wanted to describe differences in these treatment outcomes with HIV negative patients. I used record review for this purpose. I further wanted to see what the barriers and facilitators of adherence to TB treatment in co-infected patients on concomitant treatment are from both patients' and health workers' perspectives, because it would not be possible to extract such information through reviewing records, and it would also help explain the findings of the quantitative study. In addition, by using in-depth interviews, I was able to address the multiple factors that might be involved in adherence to treatment, which were also contextualized. As I described above, assessing adherence would need assessing complex factors which include provider-related factors; social, cultural, economic factors; regimen related factors. Using the focus group discussions helped explore my objectives further and also helped me validate the results of the interviews.

### **2.3. Inclusion criteria**

For the record review, records of all patients 16 years (cut off age for adult in treatment centers) and above registered for TB treatment during the inclusion period (July 2006-September 2007) and who concomitantly received ART while on TB treatment were reviewed.

For the HIV negative group, records of consecutive patients 16 years and above and treated for TB were included, starting from the initial period of inclusion (July 2006).

The inclusion criteria for patients participating in the in-depth interviews were:

- Age 18 years and above
- Treated for TB and received ART while on anti-TB treatment
- Treatment outcome known from TB register at the clinic

For the focus group, the inclusion criteria were:

- Age 18 years and above
- On treatment for TB, has taken drug for at least two months
- Is receiving concomitant ART

In addition, health professionals in the three clinics who were actively involved in the management of co-infected patients were also included.

#### **2.4. Exclusion criteria**

Records of patients below 16 years and charts of patients for whom the diagnosis of TB was changed before treatment completion were excluded.

Patients who were less than eighteen years old, who were unwilling to participate, who were not mentally fit, and for whom the diagnosis of tuberculosis was changed before completion of treatment were excluded from the interviews and focus groups.

#### **2.5. Study population**

Our study population for the quantitative study was patients who had been registered for TB treatment in our period of inclusion and who concomitantly received ART in the three health centers we included. All co-infected patients on concomitant treatment in the period of inclusion were included if they fulfilled the inclusion criteria. We included all consecutive HIV negative patients registered for TB treatment starting from the period of inclusion onwards until the same sample size as the HIV negatives was reached.

The study population for the in-depth interviews and focus groups was also selected from the three health centers. Six patients from Bole Health Center, five from Arada Health Center and four from Woreda 7 Health Center were recruited for the interviews. The numbers were determined by how many patients the health professionals were able to recruit for me from the respective health centers. For the focus group discussions,

patients were recruited from two health centers; the participants in the male group were selected from Arada Health Center and those in the female group from Bole Health Center. It was most convenient for patients to come to the health center where they were being treated and that was the reason why the focus groups were constituted of patients from the same health centers. The nine health professionals interviewed were recruited from all three health centers. The following tables (1-3) show the characteristics of the patients interviewed.

<b>Table 1. Characteristics of patients interviewed</b>	
Characteristic	No.
<i>Gender</i>	
Male	7
Female	8
<i>Age</i>	
< 25	3
26-35	4
> 35	8
<i>Education</i>	
Illiterate	3
Read and write	3
Primary school	4
Secondary school and above	5
<i>Occupation</i>	
Unemployed	4
Civil servant	1
Private	2
Other*	8
<i>Treatment outcome</i>	
Successful treatment completion	6
Default	6
Re-treatment	3
* Includes patients with irregular jobs	

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**Table 2. Characteristics of health professionals interviewed**

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Characteristic	No.
<i>Gender</i>	
Male	3
Female	6
<i>Profession</i>	
Clinical nurse	6
Health officer	2
Doctor	1
<i>Work experience</i>	
< 5 years	1
5-10 years	2
> 10 years	6

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**Table 3. Characteristics of focus group participants**

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Characteristic	No.
<i>Gender</i>	
Male	7
Female	7
<i>Age</i>	
< 25 years	2
25-35 years	7
> 35 years	6
<i>Occupation</i>	
Unemployed	3
Civil servant	2
Private	5
Other	4

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## **2.6. Data collection methods**

The methods for data collection were both quantitative and qualitative. The use of this combination of methods allowed me to explore all my objectives in depth. Through the use of record reviews, I was able to see what proportion of patients defaulted treatment, as well as what proportion had the other different treatment outcomes. In addition, I was able to see whether some recorded variables from the patients chart could be predictors of adherence or non-adherence in these patients. In addition, I was able to describe differences in treatment outcomes with HIV negative patients. But many factors would be left unexplored if my study did not have the qualitative component, most importantly the experiences of drug intake of patients from their own perspective, including how concomitant illness, concomitant treatment, the health services provided etc are perceived and how they influence adherence. I used different groups of patients and I also included health professionals to get different perspectives and explore the different factors that could influence adherence.

## **2.7. Sample selection**

I first contacted the Regional Health Bureau and I was able to determine all the health centers from which I could choose three health centers in which to conduct my study. I estimated roughly the total number of patients I could get from one health center in the inclusion period after contacting health professionals and I estimated that three health centers would be enough to reach my sample size, which ended up being the case. Then I selected the three health centers from the 21 health centers by using the lottery method, and Bole Health Center, Arada Health Center and Woreda 7 Health center were selected.

For the interviews, I used purposeful sampling. Sampling in qualitative methods is done to enhance and saturate theoretical sensitivity through strategic sampling, and not random sampling, as is the case with quantitative studies. This should result in adequate diversity and breadth of the matter that we want to analyze (51). Thus, I selected patients with different experiences (successful completion of treatment and default; as well as new patients and patients with previous history of treatment for TB, patients currently on treatment), different age groups, from both sexes and with differing socio-economic

status. In addition, I also tried to include patients for whom ART was started at different stages during TB treatment. (before anti-TB initiation, in intensive phase, in continuation phase).

It was quite difficult to get hold of defaulters because they totally disappeared from the health system, often abandoning simultaneously their ART treatment, hence, in the case of defaulters, I included those defaulters the health professionals could find for me without looking for the age, sex, socioeconomic etc. diversity I looked for in the other patients.

In addition, as my aim was to explore barriers and facilitators of treatment adherence, I did not limit my study to the study of defaulters or put particular emphasis on them. Rather, I believed that it was important to include the experience of both defaulters but also patients who had successfully completed treatment. Both defaulters and those with successful treatment completion might have their own barriers and facilitators, and what leads them in either direction (completing treatment or defaulting from treatment) might be the type of balance that is eventually reached and which factors are predominant; and I wanted to explore that. Similarly, it is very important to explore the experience of new patients and those on re-treatment because patients on re-treatment constitute a large proportion of TB patients in the HIV era, and might have different experiences from that of the new patients. The literature on concomitant treatment also points to the fact that the timing of ART during the course of TB treatment can potentially affect adherence. Hence, I also wanted to explore the experiences of patients initiated on ART at different times.

When I first contacted the health professionals who did the patient recruitment for me, I explained to them that I wanted the above mentioned diversity in the patients, in addition to the inclusion criteria; I was also contacting them repeatedly to inform them of the patients I had interviewed in all three health centers and which patients I further wanted to interview.

I conducted the focus group after I finished my in-depth interviews. My aim was to discuss factors that I felt needed further exploration but mainly to validate the results of my interviews by bringing forward issues discussed in the in-depth interviews. I selected patients who had been on treatment for TB for at least two months and were concomitantly on ART. I tried to create homogeneous groups as much as possible. I created groups with males only and with females only because I believed the cultural set up would restrain the females from talking if they were put together with men. Additionally, to make the groups as homogeneous as possible, I asked the health professionals to avoid extremes of age, again because, in the Ethiopian culture, age creates a certain hierarchy and younger people are usually supposed to listen when older people talk; but I was also afraid of the relationship between age and HIV infection and how it could affect the discussion. Although variations in other factors such as socio-economic status, level of education etc could also be thought to influence the discussion, it would be quite difficult to create homogeneous groups with respect to all such factors, but I tried to create groups that are as homogeneous as possible.

I chose patients who were on treatment for the focus group for two reasons: the first is the fact that these patients will be sharing lived experiences of their illness and drug intake, share their day to day struggles while still experiencing them; it also offers the advantage of avoiding recall bias. In addition, it is easier to contact these patients as opposed to finding patients who have already left the health system, or are only coming infrequently to collect their ARV drugs.

## **2.8. Sample size**

For the quantitative study, the sample size was calculated using the formula used for determination of sample size for estimating single proportion:

$$N = Z^2 P (1-P) / E^2$$

Where  $Z = 1.96$

$P$  = rate of non-adherence (default) to anti-tuberculosis treatment

$E$  = allowable error



Hence, based on a previous study conducted in Ethiopia where they found a default rate of 18% (32), with confidence interval of 95% and taking a margin of error of 5%, I found a sample size of 227. And when 10% was added for exclusions from final analysis (death, failure, transfer out), the sample size was 249.

My eventual sample size was 248 patients, after including all the co-infected patients initiated on treatment within the inclusion period in the three health centers; I similarly included the same number of HIV negative TB patients.

For the in-depth interviews, I included fifteen patients and eight health professionals. I included fourteen patients in the focus group discussions, with seven patients in each focus group. This is the number of patients and health professionals I believed was sufficient in exploring my subject of interest in depth, with saturation reached.

## **2.9. Procedure for data collection**

My first step after getting to Addis-Abeba was to go to hospitals providing free ART service to check whether the data I was looking for was available. I visited three hospitals and I found out that the treatment outcomes of TB were not recorded for many patients who had been treated in the ART clinic, although, for most patients, the TB treatment initiation was noted. These hospitals do not have TB clinics and the patients are sent to their closest health center for TB treatment.

Then, I started going to health centers where ART treatment was being provided and checked whether I could find the treatment outcomes. Although again the treatment outcomes for TB were not registered for all patients in the ART clinics, since the patients received their TB treatment in the same health center, I realized I would be able to trace the patients in the TB clinic based on the date of TB treatment start, the full name and the age of the patient present on the ART charts. I therefore decided to conduct my studies in the health centers.

Thereafter, I contacted the Addis-Abeba Health Bureau for Ethical Clearance, and, after receiving my ethical clearance, I contacted the medical directors of the respective health centers I worked in, informed them of my study and asked for permission to work in their health center. After I got the permission from the health centers, I decided I would do the quantitative data collection in two of the health centers myself and that I would need one data collector in one of the health centers. I then found one clinical nurse with seventeen years of experience to collect the data in Bole Health Center where he works in the TB clinic. Together, we went through my recording form which we modified slightly from the initial version I had prepared based on the exact information we could extract from the ART charts and the TB charts. We filled five forms together and I also checked five forms that he filled at the beginning and then he continued working in Bole health center and I worked in the remaining two health centers.

After completing my quantitative data collection, I contacted the health personnel at the TB and ART clinic and asked them to invite patients for me, provided them with the invitation form and discussed with them about the contents of the invitation form, and mainly emphasized that they should make sure that the patients understood that the participation in the study is voluntary. When I met patients that had been invited by health professionals, at their time of convenience, I also further discussed the issue with them, explaining to them that participation is voluntary and will not affect their treatment; that confidentiality will be ensured; and I explained the purpose of the study and my role. I invited the health professionals myself and similarly discussed the purpose of my study and the conditions for participation with them as well.

Then I pre tested my interview guide on two patients and modified it slightly from the original version because some questions were too vague and elicited “what do you mean?” type of questions from the patients. After modifying my interview guide, I continued with my qualitative data collection.

## **2.10. Data description**

We used a recording form as a data collection tool for the quantitative component and we used in-depth interviews and focus group interviews as tools for qualitative data collection.

The recording form for the HIV positive patients included socio-demographic variables, as well as clinical characteristics such as type of TB, bacilloscopy status, CD4 count at the time of anti-TB treatment initiation, WHO stage of HIV disease, ART regimen used, whether PCP prophylaxis was given, whether there was any documented side effect while the patient was on TB treatment, whether there was any concomitant illness (other than TB and HIV) during the TB treatment period. This information was gathered from the ART charts of the patients. For the HIV negative patients, the only variables that we could record were the age, sex of the patient, site of TB and bacilloscopy status for those with pulmonary TB since these are the only information available on the TB registers.

For both groups of patients, we also recorded the treatment outcomes of cured, completed treatment, died, defaulted, failed, transferred out, as defined in the TB clinics(as per the WHO criteria).

The in-depth interviews were conducted using an interview guide, which was semi-structured with open-ended questions, and I tried to explore the knowledge of the patients about TB and about co-infection; the knowledge and attitude towards TB treatment as well as concomitant treatment and how these affect treatment; whether they have taken alternative treatment; the perceived barriers to treatment; the perceived facilitators of treatment; and I probed patients whenever necessary to explore factors that could potentially affect adherence for e.g. stigma, pill burden, attitude of health personnel... if they did not raise these points themselves. Although this was what I initially put in my interview guide, issues that came up in one interview were also explored in the following ones when necessary; hence, the interview guide was not strictly followed with some questions being left out and others added during the conduct of the study.

For the focus groups, the questions/topics that were raised were similar but they were mainly based on my findings from the in-depth interviews, since I was trying to discuss further matters that I thought needed further exploration and I was at the same time trying to validate my findings from the in-depth interviews.

## **2.11. Quantitative data collection**

I used a recording form to collect data from the patient charts. For the HIV positive cohort, I recorded information from the ART charts and the TB treatment register. Before leaving for field work, I had prepared my recording form which I had to transform slightly after revising the ART charts and looking at what information was exactly available in the charts. For the HIV negative group, I recorded information from the TB register only.

### **2.11.1. Definition of variables**

**2.11.1.1. Dependent variables (the definitions used are those used by WHO, also adopted by the Ethiopian TLCP)**

- 1. Cured:** A initially smear positive patient who is sputum smear-negative at, or one month prior to, the completion of treatment and on at least one previous occasion (usually at the end of the 2<sup>nd</sup> or 5<sup>th</sup> month)
- 2 .completed treatment:** a patient who completed treatment but for whom smear results are not available at 7<sup>th</sup> month or one month prior to the completion of treatment. (This definition applies for pulmonary smear positive and smear negative patients and to patients with extra-pulmonary disease.)
- 3. Died:** a patient who died from any cause during treatment
- 4. Failed:** a patient who remains or becomes again smear positive at the end of five month or later during treatment. Or a patient who was PTB-negative at the beginning and turned out smear-positive at the end of the intensive phase.
- 5. Defaulted:** a patient who has been on treatment for at least four weeks and whose treatment was interrupted for 8 or more consecutive weeks.

**6. Transferred out:** a patient who started treatment and has been transferred to another reporting unit and for whom the treatment outcome is not known at the time of evaluation of treatment results.

**8. Successfully treated:** a patient who was cured or who completed treatment (13).

#### **2.11.1.2. Independent variables**

**Age:** in years

**Sex:** male/female

**Marital status:** classified into single/married/divorced/widowed

**Level of education:** classified into illiterate /writes and reads/primary/secondary/higher education

**Stage of HIV:** as per the WHO staging of HIV, patients with HIV diagnosed with pulmonary TB fall in stage III and would fall in stage IV in the presence of stage IV conditions; those with extra pulmonary TB are classified in stage IV.

**Site:** classified into pulmonary/extra-pulmonary

- **Pulmonary case:** a patient with tuberculosis disease involving the lung parenchyma
- **Extra pulmonary case:** a patient with tuberculosis of organs other than the lungs (pleura, lymph nodes, abdomen, genitourinary tract, skin, joints, bones, meninges)

Diagnosis should be based on one culture positive specimen; or histological evidence from a biopsy; or strong clinical evidence consistent with active extra pulmonary disease, followed by a decision by a clinician to treat with a full course of anti tuberculosis therapy. A patient in whom both pulmonary and extra pulmonary tuberculosis had been diagnosed is classified as a pulmonary case (13).

**Bacilloscopy:** classified into positive, negative

- **Smear positive pulmonary case:** a patient with at least two initial sputum smear examinations positive for acid fast bacilli (AFB+) , or one sputum examination AFB+ and radiographic abnormalities consistent with active pulmonary TB as determined by a clinician , or one sputum specimen AFB+ and culture positive for MTB

- **Smear negative pulmonary case:** a patient with pulmonary tuberculosis not meeting the above criteria for smear positive disease. Diagnostic criteria should include: at least three sputum smear examinations negative for AFB, and radiographic abnormalities consistent with active pulmonary tuberculosis, and no response to a course of broad spectrum antibiotics, and a decision by a clinician to treat with a full course of anti tuberculosis therapy, or positive culture but three initial negative AFB sputum examinations (13).

**CD4 count at time of TB diagnosis:** CD4 count in cells per cubic millimeter of blood

**ART regimen:** regimens used for free ART service in the health centers

**PCP prophylaxis:** whether patient received prophylaxis for PCP while on TB treatment or not

**Other concomitant illness:** any illness other than TB and HIV that the patient had during the treatment of TB

**Side effect:** documented side effect to either anti-TB or ART

### 2.11.2. Quantitative data analysis

Data was cleaned, entered into a computer and analyzed using SPSS version 15. I first calculated the proportion of co-infected patients with different socio-demographic characteristics (age group, sex, level of education, marital status), site of tuberculosis, smear status, ART regimen used, presence or absence of concomitant illness, presence or absence of PCP prophylaxis and I calculated the proportion of the different treatment outcomes in these patients. I also calculated the rate of defaulting and the rate of treatment success. Similarly, I calculated the mean age, and the proportions of HIV negative patients with respect to age group, sex, site of TB and bacilloscopy status. I also calculated the proportion of the different treatment outcomes in these patients, as well as the rates of defaulting and treatment success.

For univariate analysis, I used the Chi square test to compare group differences and I used the Fisher's exact test when indicated. I also used the Chi square test to compare the treatment outcomes among the HIV positive and the HIV negative patients. I used simple

logistic regression to estimate odds ratios and confidence intervals. I used the independent sample t test to compare differences between means.

I performed multiple logistic regression analysis to assess the relative impact of predictor variables on the outcome variables and I considered a P value of 0.05 as statistically significant. In the multivariate analysis, I chose those factors for which I found a P value of less than or equal to 0.25 on univariate analysis and also chose variables which I strongly suspected to have association.

## **2.12. Qualitative data**

### **2.12.1. Data collection**

#### **2.12.1.1. Interviews**

I begun my interviews after I finished my record reviews, after doing a preliminary analysis of the quantitative data so as to see factors that needed to be further explored or clarified. For example, one of the findings from the quantitative data that I particularly found interesting was that, as opposed to my assumption/hypothesis, there did not seem to be a highly significant difference in the rate of default from TB treatment between co-infected patients on concomitant treatment and HIV negative patients and I believed that I needed to explore the reason behind that further. In addition, while conducting the quantitative data collection, I managed to establish good contact with the health personnel at the health centers, and I also engaged in informal discussions with them, which was later important for my qualitative data collection. In addition, I managed to conduct some observation at that time, trying to observe factors such as patient- provider contacts, the duration of contacts, waiting times for patients...Although observation was not a major part of my study, it not only helped me familiarize with the setting, but mainly allowed me to formulate further discussion points and allowed me to see some points from a different angle than I initially did.

When I was ready for the interviews, I asked the health professionals to appoint patients for me, as per the criteria I discussed earlier. The patients were appointed at their time of convenience and I conducted the interviews in clinic offices which were empty at the

time of my interviews. Health professionals were also interviewed in their offices at their time of convenience. I used an interview guide, and I tried to formulate my questions in a way that they were simple and clear and not leading. I did not follow the interview guide strictly, and I added and/ or subtracted questions as more interviews were conducted since I wanted to discuss further issues that came about in one interview and leave points that I thought were already well explored. The interview guide was particularly important in helping me check whether I covered all my topics of interest. The interview guide was initially pre-tested on two patients, and questions that were poorly understood by patients were modified accordingly.

The interviews lasted mostly from 45 minutes to one hour and were tape recorded, except two occasions where patients were uncomfortable with the recording and I had to stop the recorder and take note of the interviews. In those cases, although the patients did not completely decline the recording, they were asking me questions about the need for being recorded, and although I explained again thoroughly about why I was using a tape recorder, I gathered that the patients were not completely comfortable with being recorded, which I thought would also affect the information they would give me. So, I asked them whether it would be better if I did not use the recorder which they said yes to and instead, I took a note of the interviews in these cases.

#### **2.12.1.2. Focus group discussions**

The two focus groups were conducted towards the end of the data collection, after the interviews were completed. While going through individual interviews, I noted points/ themes that I thought needed to be further explored or clarified in the focus group discussions. I then formulated a set of questions based on that. Those questions were brought up for discussion in the focus groups. The focus group discussions lasted 1.5 hours on average and were tape recorded.

I chose two health centers, to conduct one focus group in each. That because I believed that patients would want to be interviewed in a setting they're familiar with, that's the health center they're attending; in addition, since the health centers are located relatively



close to the patients' residence, it would be more convenient to the patients to come there than going to another health center; thus, I couldn't mix and interview patients from all three health centers. We fixed a date with the health professionals, and willing patients were invited for participation. The focus groups were also conducted in an office in the respective health centers which was empty at the time.

### **2.12.2. Analysis**

After conducting the interviews, I transcribed the data as early as possible, so as to be able to remember the general context in which the interview was conducted and to make use of small notes that I took during the interviews such as for example notes concerning patients' emotions etc. I then translated the interviews from Amharic to English. Focus groups were similarly transcribed and translated to English.

All transcriptions were manually coded. Material about participants' perceptions about TB/HIV, perceived barriers and facilitators of TB treatment adherence were identified and coded according to Giorgi's phenomenological analysis, modified by Malterud (91). The analysis followed four steps: reading the entire material to get a sense in the whole; identifying units of meaning that represent different aspects of participants' perceived barriers and facilitators to adherence, and coding for these; condensing and summarizing the content of each of the coded groups; synthesizing and integrating the insight from the condensed meaning units into generalized descriptions and concepts concerning barriers and facilitators to TB treatment.

### **2.12.3. Inspirations for the study**

According to my literature review on adherence in general and on adherence to TB treatment in particular, and also according to my own pre-understanding, adherence is a complex phenomenon, and is influenced by many factors such as patient related factors, provider related factors, regimen related factors, socioeconomic factors, cultural factors, structural factors. And once we commit into studying adherence, all these factors should be looked into, unless one wants to focus on a specific aspect of adherence.

In search of theoretical inspiration for my study, I came across health behavior theories/models, and in particular those used in relation to adherence e.g. health belief model, theory of reasoned action, health decision model and others (92, 93). These theories/models display their own strengths and weaknesses in terms of predicting adherence in different contexts, but, as Becker notes, there are many similarities between the different theories/models. Based on this, Cummings and his colleagues abstracted 109 variables from 14 existing models which were given to the major developers of these models, to arrange those into conceptually similar categories and six summary categories eventually emerged:

1. Items pertaining to accessibility of health services, such as the individual's ability to pay for health care and awareness of health services, and availability of health services
2. Items dealing with the individual's attitude toward health care, such as beliefs in the benefit of treatment and beliefs about the quality of medical care provided
3. Items concerning the threat of illness, such as the individual's perception of symptoms and beliefs about susceptibility to, and consequences of, disease
4. Items pertaining to knowledge about disease
5. Items dealing with the individual's social interactions and with social norms and social structure
6. Items on demographic characteristics (social status, income and education)

According to Becker, the different categories assume different importance depending on the situation (or disease, or regimen) in terms of their effect on adherence (92).

I have been further inspired by Kleinman, who points out that, in all societies, health care activities (illness, the responses to it, individuals experiencing it and treating it, and the social institutions relating to it) are more or less interrelated, and need to be studied as socially organized responses to disease that constitute a special cultural system: the health care system. The health care system includes people's beliefs and behavior, which are governed by cultural rules, and are influenced by particular social institutions (e.g. clinics, hospitals, professional associations), social roles (e.g. sick role, healing role), interpersonal relationships (doctor-patient, patient-family), interaction settings (e.g. home,

doctor's office), economic and political constraints, and other factors, most notably available treatment interventions and type of health problem (94).

According to Kleinman, health care is defined as a local cultural system which consists of three overlapping parts: the popular, professional and folk sectors. The popular sector, the largest part of the system, is a matrix containing individual, family, social networks, and community beliefs and activities. It is where illness is first defined and health care activities initiated. The cognitive and value orientations of the popular culture determine when people resort to folk or professional practitioners. After receiving treatment, patients go back to the popular sector to evaluate it and decide what to do next. The professional sector is comprised of the organized healing professions, that is modern scientific medicine and professionalized indigenous medical systems. The folk sector or non professional, non bureaucratic sector involves folk medicine which is divided into sacred and secular parts. The three sectors interact because patients pass through them. The importance that the three parts play differ in different set ups, based on people's beliefs as well as the availability of the professional/folk sector. Kleinman further points out that the professional sector usually ignores the presence of the other two sectors as elements of health care, resulting for instance in patient physician relationships characterized by the physician being thought as being the most knowledgeable and the patient being a passive recipient of whatever he is told by the provider(94).

Knowledge of these different components of the health care system is important with regard to adherence because the patient's medication intake and his adherence to treatment will be affected by what happens in these different parts of the health care system, the importance that the patient gives to these parts of the health system, the time spent within those systems....

#### **2.12.4. Reflexivity**

In her account of challenges associated with qualitative research, Malterud states that: "A researcher's background and position will affect what they choose to investigate, the angle of investigation, the methods judged most adequate for this purpose, the findings

considered most appropriate, and the framing and communication of conclusions.” She further discusses that the effect of the researcher should be assessed and shared (95).

I would describe myself as both an insider and an outsider in this study. An insider, because I could understand local cultures and norms and communicate fluently with my participants since I’m from Addis-Abeba myself, and an outsider because I’m a public health student with background in medicine, which is not shared by my participants. I conducted this study as a public health researcher interested in looking at the experiences of treatment in patients with co-infection on concomitant treatment, and particularly their adherence to TB treatment while receiving concomitant therapy. My background is being a medical doctor, with some short previous experience working with HIV patients in Addis-Abeba. When I initially presented myself to the staff at the health centers, I introduced myself as a master student doing research as part of my thesis, but often times, they would ask me what my background is either at the beginning or some time after during my data collection. I had prepared an invitation for patients where I explain that I am a master student doing research, but, in almost all the cases, I would find out that the health professionals have informed the patients that I’m also a doctor.

The main reason why I wanted to present myself just as a researcher, and not a medical doctor, especially for patients, was that I did not want them to think that I’m a health professional trying to assess their medication intake; or that I was in some way part of the health system they were being treated in. I believed that would make them doubt the confidentiality of the discussions as well as its purpose and would affect the information they would be willing to give. That is why I emphasized on my role in the study, explained that I was in no way part of the clinics they were treated in and explained that their information will be treated with confidentiality and that it would not affect further treatment in any way. Often times, patients would ask me questions such as: “Can you tell me about the relationship between TB and HIV?”, in which case I would tell them to discuss the issue further with their treatment provider and tell them that we can discuss the issue a bit at the end of our discussion, which we often did. How the fact that I am a doctor affected my results is difficult to tell, but I believe that it can have both a positive

and a negative impact: the “normal” patient-doctor relationship that we have in Ethiopia is limited in terms of discussions and time spent with patients. Hence, patients are usually not used to having detailed conversations with health professionals and hence might find it difficult to open up and discuss matters in depth; in addition, patients might withhold some information regarding health professionals and the health system due to a belief that I might be part of the health system as mentioned above ; on the other hand, it is also possible that patients find it motivating that, being a medical doctor, I was interested in discussing matters other than their medical conditions. In some instances, I noted some comfort unfold in the process of interviews with patients calling me “my daughter”, instead of “doctor”, which they said at the beginning.

Similarly, I tried to establish a good relationship with the health professionals in the health centers, during my quantitative data collection as well as afterwards. We had informal discussions which were quite informative but also allowed me to explain the aim of my study in depth, and familiarize them with the fact that I was there as a researcher and not as a health professional, since I had at times the impression that they were treating me more as a colleague than as a researcher that was there for the purpose of the study. Being from the same profession, I believe, allowed us to easily bond and communicate, but, in few instances, I felt that health professionals were trying to give a medical perspective to many issues, probably hypothesizing that it is my perspective of interest.

I believe that the fact that I am a female might also have had some impact on the relationship I tried to establish with patients, mainly in that it probably allowed the female participants to talk more freely than if they had been talking to a male researcher. I also felt that my gender did not affect my discussion with male participants, probably because my gender was masked by my profession.

I also came in this study with my own pre-understandings/ perceptions. That was largely a result of the literature review that I made on my topic and partly a result of my experience working with HIV patients in the past. I therefore started this study with the

assumption that several factors would act as barriers to TB treatment in co-infected patients on concomitant treatment, more so than what has been found in patients without co-infection, because of additional factors such as high pill burden, double stigma...but I also believed that many of the factors acting as barriers and facilitators of treatment adherence would be similar in all patients. In addition, I also had the assumption that there might be misunderstandings about co-infection, and possibly concomitant treatment, and was interested in seeing how these affected patients' treatment. This might have had an impact on the way I formulated my questions and the way I perceived patients' responses, but I tried to be aware of the presence of my pre-understandings and not let that bias me.

### **2.13. Data quality**

Data quality was assured through:

1. Thorough review of charts with consultation of the health professionals for unclear matters: when I came across points on patient charts I was not clear with, I discussed those points with the health professionals in the respective clinics, and they clarified them for me. I also told my data collector to do the same.
2. Proper training and supervision of my data collector: my data collector and I went through few records together at the beginning of the data collection so that he understood clearly the points I wanted him to retrieve. I randomly checked few patient charts at the end of his data collection to see if the data gathering was done the way I wanted it to be done.
3. Pre testing of the interview guide: I pretested my interview guide and modified it accordingly before using it to interview my patients.

### **2.14. Communication of results**

The results of the study will be presented at the Institute of General Practice and Community Medicine, University of Oslo. The results, together with my recommendations, will also be submitted to the Addis-Abeba Health Bureau as well as to the respective health centers I worked in. An article will also be written and submitted to a journal.

Through informal discussions with health professionals in the health centers, I tried to point out some facts from my data collection such as the misunderstandings about co-infection and modes of TB transmission, because I believed that it might create some awareness among the health professionals who can act upon it for instance through better health education of the patients.

## **2.15. Ethical considerations**

Ethical clearance for the study was obtained from the Norwegian Ethics Committee and the Ethical Committee of Addis Ababa health bureau.

Standard coding procedures were applied for the record review so that no patient record can be traced back at a later time.

Patients were recruited through health professionals who provided them with an invitation on my behalf. I contacted those who agreed to participate at their time of convenience and provided them with all necessary information. That is, I explained again that participation is voluntary and that it will not affect treatment, that confidentiality will be assured, and I further explained the objectives of the study and I conducted the interview/focus group discussion upon their consent.

Patients who were very sick were excluded from the interviews/focus groups. The interviews lasted from 45 minutes to 1 hour and were conducted at the time of convenience of the patient, in a room where only I and the participant/s were present. All patients were refunded for their transportation costs; all received the same amount of money.

I discussed with patients who had defaulted treatment or who were contemplating it about the consequences of defaulting treatment and I tried to convince the defaulters to go back to treatment. This was done with confidentiality, and was not discussed with the health professionals.

We will first present the results of the quantitative component of the study, and then the results of the qualitative study.

### **3.1. Results of the quantitative study**

This section will be divided in two parts. In the first part, we will discuss the results of the HIV positive cohort. We will then discuss the results of the HIV negative group and present the comparisons.

#### **3.1.1. Results of the HIV positive cohort**

In this section, we will present the socio-demographic as well as clinical characteristics of the study population, and present the TB treatment outcomes. We will then present the different factors associated with defaulting from TB treatment, presenting results of both univariate and multivariate analysis.

##### **3.1.1.1. Socio-demographic characteristics of the study population**

There were a total of 248 TB/HIV co-infected patients who were initiated on TB treatment in the inclusion period (July 2006- September 2007) and received concomitant treatment. The socio-demographic and clinical characteristics of the study population are summarized in table 1. The proportion of females was slightly higher than those of males, with a female to male ratio of 1.2:1. The mean age was  $34.9 \pm 8.8$  SD, with a median age of 34. The mean age for females was 32.6 and that for males 37.7. Figure 1 shows the age distribution of the cohort.

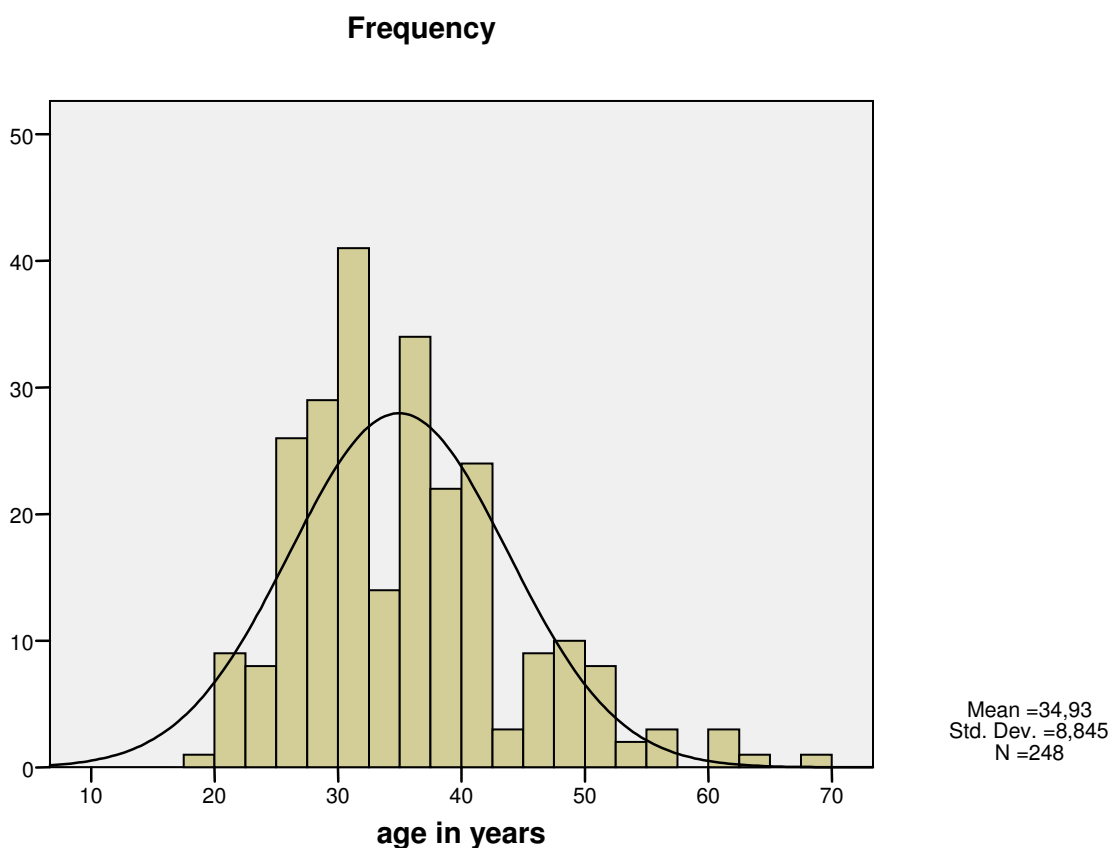
We found that 33% of patients were single, 35.5% were married, and 31.5% were either divorced or widowed. Sex related significant difference in marital status was observed ( $p = 0.006$ , see table 2), with 54 out of 136 females (39.7%) being either divorced or widowed as compared to 24 out of 112 males (21.4%); and with 40 out of 136 females (29.4%) being married as compared to 48 (42.9%) of males. The rest, that is 42 (30.9%) females and 40 (35.7%) males were single.



We found that 20.6% of patients were illiterate (had no education, could not write and read). There was a sex related difference in illiteracy status ( $p= 0.026$ , see table 2), with 16 out of 112 males (14.3%) being illiterate versus 35 of 136 females (25.7%).

**Table 1. Socio-demographic characteristics of the study population**

Characteristic	Group	n (%)
Sex	Male	112 (45.2%)
	Female	136 (54.8%)
Age group	16-24	18(7.3%)
	25-34	110 (44.3%)
	35-44	83 (33.5%)
	45+	37(14.9%)
Marital status	Single	82 (33 %)
	Married	88(35.5%)
	Divorced or widowed	78 (31.5%)
Level of education	Illiterate	47(19%)
	Read and write	4(1.6%)
	Primary	77(31%)
	Secondary	99(39.9%)
	Higher education	21(8.5%)



**Figure 1. Age distribution of the study population**

**Table 2 Comparison of males and females with regard to marital status and education**

Variable	Male	Female	Total	P value
Marital status				0.006
Single	40(35.7%)	42(30.9%)	82(33.1%)	
Married	48(42.9%)	40(29.4%)	88(35.5%)	
Divorced and widowed	24(21.4%)	54(39.7%)	78(31.5%)	
Education				0.026
Illiterate	16(14.3%)	35(25.7%)	51(20.6%)	
Literate	96(85.7%)	101(74.3%)	197(79.4%)	

### **3.1.1.2. Clinical characteristics of the study population**

We found that 162 (65.3%) patients had pulmonary TB, the rest having extra pulmonary disease. Of those who had pulmonary TB, 106(65.5%) were cases of smear negative TB.

We also retrieved data on the WHO stage of HIV at time of TB diagnosis. We found that 148(59.7%) of patients were in WHO stage III, with the rest (100 patients) falling in WHO stage IV of disease. This means that of the 162 patients with pulmonary TB, 14 had or have had a stage IV defining illness.

We also recorded the CD4 count at the time of TB treatment initiation and we found that 151(60.9%) patients had CD4 count between 50 and 200. Those with CD4 less than 50 were 44(17.7%) and those with CD4 greater than 200 were 53(21.4%). We did not record the absolute CD4 number of the patients; hence we were not able to calculate the mean CD4 count.

The continuation phase of anti-TB treatment was the most common time for initiation of ART in these patients, with 110(44.4%) patients started on ART in this phase; followed by the intensive phase, with 94(37.9%) patients initiated on ART in this phase. Forty four (17.7%) patients were already on ART when they were diagnosed with TB and started on anti-TB treatment.

Four ART regimens were used in the treatment of these patients. The regimen containing stavudine, lamivudine and efavirenz was used in 138(55.6%) patients, whereas the regimen containing stavudine, lamivudine, nevirapine and that containing combivir, efavirenz were similarly used in 46(18.5%) patients. The rest of the patients, 18(7.3%) received the regimen containing combivir and nevirapine.

Concomitant illness (other than TB and HIV) was documented in 119(48%) of patients. The three most commonly recorded concomitant illnesses were: diarrhea, candidiasis and

upper respiratory tract infection, 18% of the patients had more than one concomitant illness. Table 3 summarizes the clinical characteristics of the patients.

All patients received co-trimoxazole as PCP prophylaxis during anti-TB treatment, with three patients who were discontinued from treatment due to drug induced allergy.

### 3.1.1.3. Tuberculosis treatment outcomes of the study population

The TB treatment outcomes for the 248 patients included were as follows: 148(59.7%) completed treatment, 32(12.9%) were cured, 31(12.5%) died, 3(1.2%) failed (all three were recorded as being cases of MDR TB); twenty six patients (10.5%) defaulted treatment, and 8 patients (3.2%) were transferred out. Fig.3 illustrates the flow of the study participants.

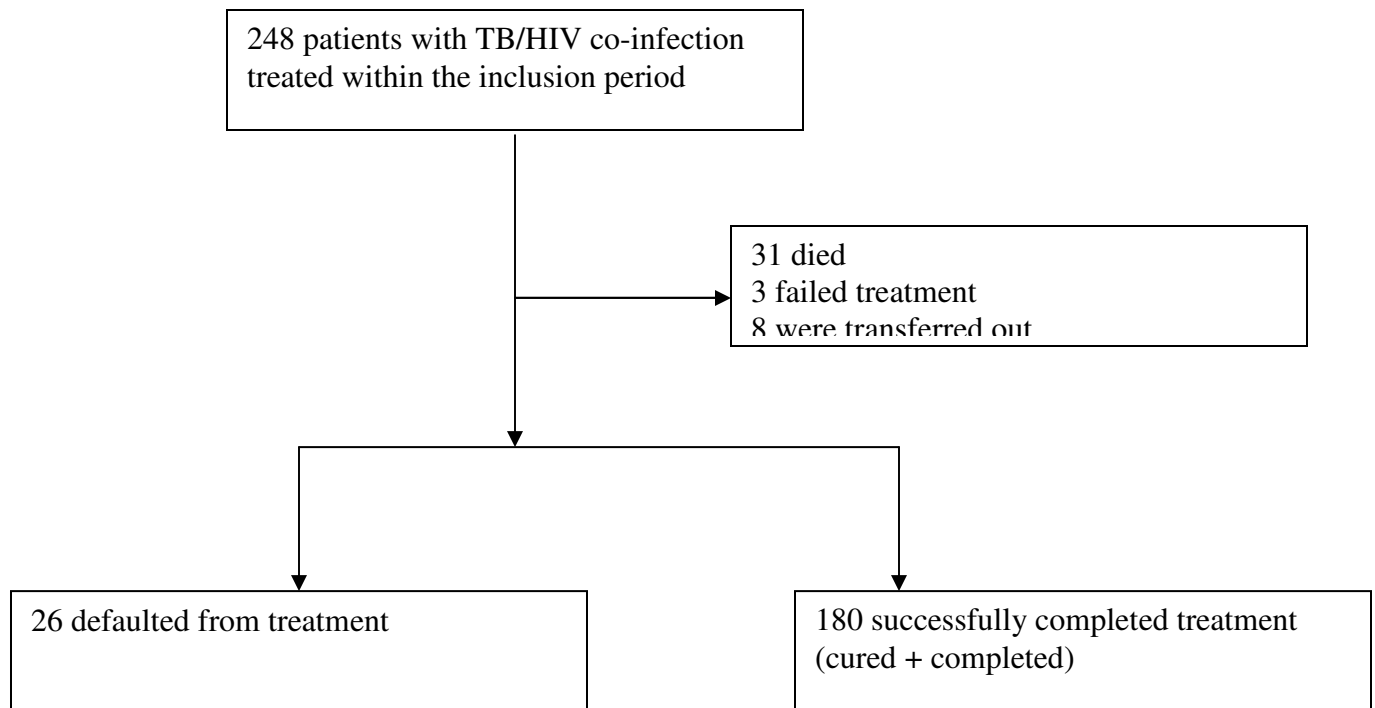
A total of 180 (72.5%) patients either achieved cure or successfully completed treatment and the default rate was 10.5%, and it was 10.7% in smear positive cases. Table 3 summarizes the treatment outcomes.

Of the 26 patients who defaulted treatment, 19 did so in the continuation phase of TB treatment, 7 defaulted in the intensive phase.

**Table 3 Clinical characteristics of the study population**

Characteristic	Group	n (%)
WHO stage	III	148(59.7%)
	IV	100 (40.3%)
Site of illness	Pulmonary	162(65.3%)
	Extra-pulmonary	86(34.7%)
Bacilloscopy status for pulmonary TB cases	Positive	56(34.5%)
	Negative	106(65.5 %)
CD4 count	<50	44(17.7%)
	50-200	151(60.9%)
	>200	53 (21.4%)

Time of ART initiation	Before start of anti-TB	44(17.7%)
	In intensive phase	94(37.9%)
	In continuation phase	110(44.4%)
ART regimen used	Stavudine/lamivudine/nevirapine	46(18.5%)
	Stavudine/lamivudine/efavirenz	138(55.6%)
	Combivir/Nevirapine	18(7.3%)
	Combivir/Efavirenz	46(18.5%)
Concomitant illness	Yes	119(48%)
	No	129(52%)



**Fig.3 Flow chart of study participants**

**Table 3. Tuberculosis treatment outcomes of the study population**

Characteristic	Group	n (%)
Treatment outcomes as per WHO criteria	Cured	32(12.9%)
	Completed	148(59.7%)
	Died	31(12.5%)
	Failed	3 (1.2%)
	Defaulted	26(10.5%)
	Transferred out	8(3.2%)
Timing of default	Intensive phase	7(26.9%)
	Continuation phase	19(73.1%)

#### **3.1.1.4. Factors associated with defaulting from TB treatment**

We compared the defaulters against patients who successfully completed treatment (taken as proxy of adherence according to the WHO recommendations). Age, sex, education, marital status, health facility used, WHO stage of disease, site of illness, bacilloscopy status, CD4 count, concomitant illness, time of ART initiation were all assessed for association with default using univariate analysis. The analysis showed that sex, education and time of ART initiation were associated with defaulting from TB treatment; the other variables did not show significant association. Accordingly, male sex was significantly associated with defaulting ( $p=0.046$ , OR= 2.36 (95%CI: 0.99-5.57)). Education level of primary and below was also found to be significantly associated with defaulting ( $p=0.041$ , OR=2.45(95%CI:1.01- 5.94)). Similarly, timing of ART initiation was also found to be significantly associated with defaulting from treatment ( $p=0.001$ ). The results of the univariate analysis are summarized in table 4.

**Table 4 Univariate analysis to assess association between socio-economic and clinical characteristics and defaulting**

Group	Default (%)	Successful treatment (%)	OR (C.I)	p-value
Sex				<b>0.046</b>
Male	17(17.5%)	80 (82.5%)	2.36 (0.99-5.57)	
Female	9 (8.3%)	100 (91.7%)		
Age				0.373
16-34	16(14.5%)	94 (85.5%)	1.46(0.63-3.39)	
35+	10 (10.4%)	86 (89.6%)		
Marital status				0.238
Married	7(9.1%)	70(9.9%)	0.579(0.231- 1.44)	
Non married	19(14.7%)	110(85.3%)		
Health facil.				0.522
Bole	9 (10.7%)	75 (89.3%)	0.98 (0.32- 2.92)	
Arada	11 (16.4%)	56 (83.6%)	1.60 (0.55-4.65)	
Woreda7	6 (10.9%)	49 (89.1%)		
Education				<b>0.041</b>
Primary and below	18(17.3%)	86(82.7%)	2.45(1.01- 5.94)	
Secondary and above	8(7.8%)	94(92.2%)		
WHO stage				0.543
III	15 (11.5%)	115 (88.5%)	0.77(0.33-1.77)	
IV	11(14.5%)	65 (85.5%)		
Site of illness				0.671
Pulmonary	18(13.3%)	117(86.7%)	1.21(0.49-2.94)	
Extrapulm.	8 (11.3%)	66(88.7%)		
Bacillos. status				0.765
Positive	6(12%)	44(88%)	0.85(0.29-2.43)	
Negative	12(13.8%)	75(86.2%)		
CD4 count				0.275
<50	6 (18.8%)	26(81.3%)	1.21(0.37-3.88)	
50-200	12(9.7%)	112(90.3%)	0.56(0.21-1.47)	
>200	8(16%)	42(84%)		
Conc. Illness				0.832
Yes	13 (13.1%)	86 (86.9%)	1.09(0.48-2.48)	
No	13 (12.1%)	94 (87.9%)		
Time of ART init.				<b>0.001**</b>
Before anti-TB	6 (16.7%)	30(83.3%)	4.60(1.21-17.40)	
Intensive phase	16(21.6%)	58(78.4%)	6.34(2.02-19.91)	
Contin. phase	4 (4.2%)	92(95.8%)		

\*\*Fisher's exact test

We performed multiple regression analysis to assess the possible association of different socio-economic and clinical variables with defaulting from treatment. The independent variables included in the multiple regression analysis were: sex, level of education, marital status, CD4 count, time of ART initiation.

In multivariate analysis, after simultaneously controlling for potential predictor variables, sex, education and timing of ART initiation remained independent factors associated with defaulting from treatment. Table 5 shows the results of the multivariate analysis. Males were 2.6 times more likely to default than females AOR= 2.66(95%CI: 1.05- 6.71), P=0.038. Similarly, initiation of ART in the intensive phase was significantly associated with defaulting as compared to ART initiated in the continuation phase, AOR= 9.68(95%CI: 2.71- 34.57), P= <0.001; the same was true for ART initiated before the start of anti-TB as compared to ART started in the continuation phase, AOR= 4.83(95% CI:1.19- 19.83), P= 0.025. Education also remained significantly associated with defaulting, with those with education level of primary and below having 3.81 times the chance of defaulting than those with secondary and above education. AOR= 3.81(95% CI:1.38- 10.52), P= 0.009.



**Table 5 Multivariate analysis of factors associated with defaulting**

Variable	AOR (CI)	P value
Sex		
Male	2.66(1.05- 6.71)	0.038
Female		
Marital status		
Married	0.51(0.18-1.41)	0.195
Non married		
Level of education		
Primary and below	3.81(1.38- 10.52)	0.009
Secondary and above		
CD4 count		
<50	0.99(0.25-3.81)	0.993
50-200	0.33(0.10-1.06)	0.063
> 200		
T of ART initiation		
Before anti-TB	4.83(1.19- 19.83)	0.027
Intens. phase	9.68(2.71- 34.57)	< 0.001
Cont. phase		

### 3.1.2. Results of the HIV negative group

#### 3.1.2.1. Socio-demographic and clinical characteristics of the HIV negative patients

Age and sex were the socio-demographic characteristics that were recorded at the time of anti-TB initiation in the TB clinics. Of the 248 patients included, 127 (51.2%) were females. The ratio of females to males was 1.04/1.00.

The mean age was 31.83 (+/\_14.3) and the median age was 26. The mean age of females was 30.53 and that of males was 33.19.

Pulmonary TB was documented in 144(62.5%) patients, whereas 93 patients (37.5%) had extra pulmonary disease. Of those with pulmonary disease, 78(50.3%) were smear negative. Table 6 summarizes the baseline characteristics of the patients.

### 3.1.2.2. TB treatment outcomes

We found that 57(23%) of patients achieved cure, 141(56.9%) successfully completed treatment, 10(4%) died, 1 patient failed treatment, 20(8.1%) defaulted, 19(7.7%) were transferred out.

Therefore the treatment success rate was 79.9%. Of the 20 patients who defaulted from treatment, 3 did so in the intensive phase and 17 in the continuation phase of TB treatment. Table 7 summarizes the treatment outcome of the patients.

We performed univariate analysis to assess factors associated with defaulting and we found that sex, age, site of illness and bacilloscopy status were not significantly associated with defaulting. Table 8 shows the results of the univariate analysis.

**Table 6 Baseline characteristics of the HIV negative patients**

Characteristic	Group	n (%)
Sex	Male	121(48.8%)
	Female	127 (51.2%)
Age group	16-24	96 (38.7%)
	25-34	80 (32.3%)
	35-44	27 (10.9%)
	45+	45 (18.1%)
Site of disease	Pulmonary	155 (62.5%)
	Extra pulmonary	93 (37.5%)
Bacilloscopy status	Positive	77 (49.7%)
	Negative	78 (50.3%)

**Table 7 Treatment outcomes of the HIV negative patients**

Treatment outcome	Group	n (%)
Treatment outcomes as per WHO criteria	Cured	57(23%)
	Completed	141(56.9%)
	Died	10(4%)
	Failed	1 (0.4%)
	Defaulted	20(8.1%)
	Transferred out	19(7.7%)
Timing of default	Intensive phase	3(15%)
	Continuation phase	17(85%)

**Table 8. Univariate analysis of factors associated with defaulting in the HIV negative group**

Group	Default	Successful treatment	OR (C.I)	P value
Sex				0.426
Male	11(10.9%)	90 (89.1%)	1.45(0.57-3.66)	
Female	9 (7.8%)	107 (92.2%)		
Age				0.817
16-34	15(9.5%)	143 (90.5%)	1.13(0.39-3.26)	
35+	5 (8.5%)	54 (91.5%)		
Site of illn.				0.218*
Pulmonary	16(11.2%)	127(88.8%)	1.21(0.49-2.94)	
Extrapulmonary	4 (5.4%)	70 (94.6%)		
Bacillos. status				0.556
Positive	9(12.7%)	62 (87.3%)	1.36(0.48-3.89)	
Negative	7 (9.6%)	66 (90.4%)		

\* Fisher's exact test

### **3.1.3. Comparison of the HIV positive and HIV negative groups**

#### **3.1.3.1. Comparison of demographic and clinical characteristics**

We found that there is a significant difference in the mean age ( $p=0.004$ ) between the two groups. The mean age was  $34.9 \pm 8.8$  SD in the HIV positive group and  $31.83 \pm 14.3$  SD in the HIV negatives with a mean difference of 3.1.

We performed univariate analysis to compare the HIV positive and the HIV negative groups with regard to sex, site of illness and bacilloscopy status. We found that there was no significant difference in sex between the two groups ( $p=0.418$ ). There was also no significant difference between the two groups in terms of site of disease ( $p=0.513$ ). There was a significant difference in bacilloscopy status ( $p=0.009$ ), with 106 out of 162(65.5%) patients being smear negative in the HIV positive group versus 78 out of 155(50.3%) patients in the HIV negative group. Table 9 summarizes the comparison.

**Table 9 Comparison of characteristics of HIV positive and negative groups**

Group	HIV positive	HIV negative	OR (C.I)	p-value
Sex				0.418
Male	112(48.1%)	121(51.9%)	0.86(0.60-1.23)	
Female	136(51.7%)	127(48.3%)		
Age(mean)	34.9± 8.8 SD	31.83±14.3SD	0.97(0.96-0.99)	0.004*
Site of illness				0.513
Pulmonary	162(51.1%)	155(48.9%)	1.13(0.78-1.63)	
Extrapulm	86(48%)	93 (52%)		
Bacilloscopy				0.009
Positive	56(42.1%)	77(57.8%)	0.55(0.35-0.86)	
Negative	106(57.6%)	78(42.4%)		

\* Independent sample t test

### 3.1.3.2. Comparison of treatment outcomes between the two groups

On univariate analysis, we found that there was no significant difference between the two groups ( $p= 0.261$ ) in TB treatment outcome (default versus treatment success). Table 10 presents the comparison.

**Table 10 Comparison of default between HIV positive and negative groups**

Characteristics	HIV positive	HIV negative	OR(CI)	P value
Outcome.				
Default	26 (56.5%)	20 (43.5%)	1.42(0.76-2.63)	0.261
Successful treatment	180 (47.7%)	197(52.3%)		

We performed multiple regression analysis, and, after controlling for age and sex, we found that HIV status was not associated with defaulting from TB treatment, AOR= 1.56 (95% CI: 0.78-3.13),  $p= 0.201$ . Table 11 summarizes the results.

**Table 11. Multivariate analysis to assess factors associated with defaulting**

Variable	AOR (CI)	P value
Sex		
Male	1.98(1.04- 3.77)	0.037
Female		
Age		
16-25	1.15 (0.39- 3.39)	0.792
25-34	1.26 (0.49- 3.21)	0.622
35-44	0.69 (0.23- 2.08)	0.518
45+		
HIV status		
Positive	1.56(0.78- 3.13)	0.201
Negative		

### 3.2. Results of the qualitative study

This section presents the results of the qualitative study, which consisted mainly of in-depth interviews and focus group discussions as previously discussed. But the results have also been informed by informal discussions, mainly with health professionals as well as observations made during data collection.

#### 3.2.1. Understandings/ perception about TB, TB/HIV co-infection and concomitant treatment

Participants conveyed beliefs about various causes for TB. The most common factor thought to lead to TB by the majority of patients was *bird* which literally means cold. Someone is thought to be “hit” by *bird* upon exposure to cold air and mainly blowing wind, but also upon exposure to cold water such as being exposed to heavy rain. *Bird* is believed to be a cause of illness, mainly the cause of cough but also frequently the cause of any form of muscular pain. Many patients recalled being *hit* by *bird* some time before they started coughing. A 36 years old male patient explained:

“I have been in Italy, and there is a lot of snow there, and that is what predisposed me to TB. It is very cold there, and we wear a lot of clothes, but sometimes, mainly when you are working, you forget to wear good clothes, and the bird hits you. That is why I had TB. Bird had gone into my body.”

In addition, when heat and cold “collide”, the effect is thought to be worse than when one is “hit” just by cold; and also when the wind blows through an open window or door, mainly when those are partially open, since it increases the “force” of the wind. In this case, people would say: “*draft metagn*”, which means I was hit by *draft*. A 35 years old female patient said:

“The main reason for TB is bird. Bird that diagonally goes into your body, from your sides and back, predisposes to TB, which is known. If some people are in the car and they are exposed to bird, and also sometimes because of the rain, that also gets into the body. Also, when cold and heat collide, that leads to TB also.”

My personal illustrative example related to the phenomenon of *bird* is the experiences I frequently encounter while trying to open the windows of taxis which are a common means of transportation in Addis-Abeba. Many times, that would upset most of the people in the taxi who would close the windows immediately, claiming that they do not want to be hit by *bird*, no matter how warm it is or how many people are in the taxi. This is a reflection of how *bird* as a cause of illness is deep rooted in people’s mind in Ethiopia.

All health professionals are aware of this belief and some even refer to it as “the *bird* theory.” They explain that cough and chest conditions such as pneumonia and TB are believed to be due to *bird* by many patients. A clinical nurse shared his experience at the TB clinic:

“Over 90% of people, including educated people, are saying it is *bird*, and then they say I started coughing, and it changed into TB. Even educated people say that. When we tell them, cover your mouth, they get confused. And they say, but we have been closing all windows, so then should our brother, our mother, get tested? And it is even a problem here where we work. They go and close the door, and we explain, we leave it open because of this reason.”

Other factors mentioned by patients as being potential causes of TB included: excessive sun exposure, exposure to mud, smoking, alcohol, khat, and inadequate food intake. Excessive sun exposure is also believed to predispose to illness in Ethiopia, although to a lesser extent than *bird*. In that case, people would say “*mitch metagn*”, meaning I was hit by *mitch*. Some patients had a belief that smoking, alcohol, and khat

are causes of TB from what they hear in the community and for some, this was reinforced by health professionals' prohibition of intake of these substances upon diagnosis of TB and initiation of treatment. Hence, these were perceived by some patients as being causative factors for TB, as well as aggravating factors, with patients mentioning that smoking, chewing khat and drinking alcohol would lead a patient to get TB but that they would also result in a delay in getting cured once the patient is started on treatment. The lung was thought of as a fragile organ, through which these substances pass, a "recipient of everything going into the body" as described by one patient. Lack of food or consumption of poor quality food was also thought to lead to TB by many, who believed that it was the reason for them to get TB. A 46 years old male patient said:

"Q. Do you know what causes TB?

*Bird*, sun, excess mud. That is what predisposed me to TB. In addition, you know, there is the problem of food. If you do not eat good food, you get TB. And for me, my life is from hand to mouth, so, sometimes, you have to eat beans and sleep."

Hence, TB was perceived by many as being a disease of poverty, resulting from a lack of food or consumption of poor quality food; and a body harmed by lack of food as well as hard work was thought to be more easily predisposed to *bird*. In addition, work that starts very early in the morning and work that results in excessive exposure to sun were thought to be particularly responsible for the development of TB.

Few patients mentioned bacteria as a cause of TB. Some patients mentioned transmission from another person through breathing. Sharing eating and drinking objects was also mentioned by some as a mode of transmission of TB, and patients or their families had separated their eating utensils after the diagnosis of TB. Two patients said that TB could be sexually transmitted since health professionals were telling them not to have sex during treatment. Health professionals who were asked why they were prohibiting sex during TB treatment said that it was because of the fear that patients would lose too much energy. A clinical nurse explained:

“Yes, we tell them to stop having sex. You know, you lose energy with sex, and for a sick person, it is not good. If you don’t tell them, they just do it without limits; you have to be strict with that.”

Other patients also believed that different origins and modes of transmission exist for TB, some getting it from *bird*, others from other people, that being the reason why some patients are told to cover their mouth at the clinic, and others not, and said that the drugs were also different depending on which type of TB one has.

A large majority of patients was aware that there is a relationship between TB and HIV. A common belief was that TB could change into HIV, if TB had been left untreated for long. Therefore, *bird* was most frequently thought to be the cause of TB which, due to delay in treatment, could transform into HIV. Some patients said that they had heard about this in the media. A 36 years old male patient explains how the TB changed into HIV in his case:

“Sometimes, when we sit and wait for the nurse to give us the drugs, we talk with the other patients. And they also have HIV, many have.”

Q. Why do you think many people with TB also have HIV?

I think it is because we do not come to the clinic early. Me, I was at home thinking I will get better. The cough, for me, started more than two months back. But I was drinking hot drinks at home; I thought I will get better. So I came to the clinic here late. I think that is why I got the HIV. The samba (TB) changed to HIV. If I came to the clinic earlier, maybe it would not have changed on me.”

Health professionals are aware of this belief among patients. A clinical nurse shared her experience while doing provider induced counseling and treatment (PICT).

“When I was doing PICT, I had patients who thought that you would have HIV if you have TB, they thought of the two diseases as being similar. At the beginning, when you tell them that a person with HIV would get TB because of the immunity..., they say, Ah! It’s like that? Because they thought HIV follows TB, that they will get it after the TB. There is a patient who recently told me that the TB changed on him.”

For the majority of these patients, two types of TB exist: the TB that is related to HIV (or can change to HIV), and the one that is not related to HIV. Most knew patients who had had TB even before HIV came to be known, or know patients with TB who got



treated and cured and did not have HIV even in the HIV era. The most common type of TB was believed to be the HIV related TB. Some estimated the HIV related TB to constitute as high as 90% of TB.

Other patients explained the relationship between the two illnesses as being a result of a weakness in the body due to HIV, which leads to a susceptibility to other diseases such as TB, but also diarrhea, skin lesions...

According to some health professionals, many patients who came to the TB clinic usually assumed that they could have HIV infection, before getting the test. Families accompanying patients were also strongly suspicious of the possibility of the patient having HIV when diagnosed with TB. A clinical nurse explained his experience:

“Even their (patients’) families, when you ask them, what is the problem, they would say: it is the new disease (HIV). And sometimes, you ask them, did he get tested? And they say, well, he has TB, so he has HIV. Sometimes even when we tell them they are negative, they do not trust us.”

Some health professionals associated the high acceptability of HIV counseling and testing (which some quantified as being between 70-90%) in the TB clinics to the fact that there was a widespread belief among patients that TB and HIV were associated, hence patients usually were prepared for the possibility of an HIV diagnosis. A clinical nurse said:

“What they (patients) say when we ask them to get tested for HIV is that, normally, they come here thinking that they have HIV. There is this thinking among people. They conclude that, if you have TB, you have HIV. When you ask them to get tested, they do not take it as a problem, I am positive, so it is no problem, is their attitude.”

Some patients also said that, if TB comes back (relapses), then that can be an indication of HIV infection. One of these patients was told by her relatives that, if her TB came back, then she might have the “new disease”, and was advised by them to get tested.

In contrast to the knowledge about TB, all of the patients in the study knew that HIV could be transmitted sexually and through blood containing sharp objects, such as needles. Most had gotten the information from mass media, such as radio and TV. But, when asked about the relationship between TB and HIV, many, as mentioned above would respond that TB could change into HIV; hence classifying HIV into two, the one that is transmitted from others through sexual intercourse and exposure to sharp objects, and the other that had followed TB. A 50 years old female patient said:

“It is from TB that I got this disease (HIV). They go side to side. The *samba* (TB) went into HIV. Initially, I was saying, can it be from sharp objects, but it is not. It is the *samba* that changed. I am a *menekussie* (equivalent to a nun in the orthodox religion); I did not go to a man.”

### **3.2.2. Perception of the effect of HIV on TB and its treatment**

One of my interests was to see how treatment and prognosis are perceived by patients with co-infection, how they see the impact of HIV on their TB treatment. Most patients agreed that TB could be cured, even in the presence of HIV infection; but a majority thought that it was more difficult to be cured when one was an HIV infected TB patient as compared to an HIV negative person. “Weakening” of the body by HIV was a reason mentioned by some, who explained that the two diseases support each other to weaken the body. Hence, the body was thought to need more time to heal. For others, if TB has turned into HIV, it was thought to be very difficult to treat. A 20 years old female patient explains the prognosis:

“If you have HIV, TB can be strong, because they can collide. If you do not have HIV, TB will disappear soon. Like any person who has TB, you take your drug, and it disappears, but if you have HIV, it will not disappear fast.”

Two patients also mentioned that the reason why TB treatment was given for 8 months is because it is more difficult to achieve cure in an HIV positive person, and said that treatment is shorter for HIV negative patients.

Patients had a divided opinion on which disease they thought was the most severe

when comparing TB and HIV. Some mentioned HIV as being the most serious illness that they feared more, while others thought that TB was more dangerous. Some patients also mentioned being told by health professionals that TB would kill them before HIV does if they don't take their TB treatment properly; which motivated them take their TB treatment properly. This perception of severity affected partially the decision about which drug to discontinue for those patients who decided to take one of the drugs and stop the other. A 36 years old male defaulter explains the reason why he decided to discontinue his anti-TB drugs and continue with the ART after experiencing side effects aggravated by lack of food:

“I said: I have to take at least one of the drugs. I wanted to survive. I said, I will take the HIV drugs only.

Q. Why the HIV drugs and not the TB drugs?

The HIV, it will kill you, it will kill you fast. Samba (TB) will not kill me if I take these drugs (ARV drugs) properly.”

Many patients tended to classify patients with TB as having HIV or not based on their weight status and their strength. Particular emphasis was put on weight, with thin patients classified as being HIV positive; but patients who came to the clinics looking weak or supported by others were also considered as being HIV positive by the patients. Darkening of the skin was also commonly mentioned by patients as a sign of HIV infection. A 46 years old male patient explains:

“When I see other patients in the TB clinic who do not have HIV, they are stronger than me.

Q. How do you know they are HIV negative?

I told you, they are strong. They are not like me. The two illnesses, they support each other to weaken you. Oh! Your body, your mind, they all get weak!”

### **3.2.3. Hope and survival**

A word that almost every patient used when I asked about how they felt upon diagnosis of co-infection is hope. Loss of hope was a common feeling that patients had upon diagnosis of TB followed by HIV or vice versa, despite many being suspicious of a possibility of being co-infected, when first diagnosed with TB. For many, the initial

period of diagnosis of co-infection was therefore a very tough period. Many also feared not being able to survive two illnesses. For some, it also meant that their illness had progressed and had changed into HIV, which was associated with a worse prognosis.

Two patients had also contemplated committing suicide. A 30 years old male defaulter explains:

“When they told me I had TB, I started waiting for my death. When you already have HIV, it is the worst illness you can have. You don’t want it to happen to anyone. And, if, together, they tell you that you have TB, what can you do? You lose hope. I was waiting for my death. Two diseases, it is the work of Satan! I did not think I will live after that. I was upset. That is why, after some time, I stopped the drugs and I was told I have to take them again.”

For some patients, counseling received from health professionals played a critical role in managing this difficult period. These patients explained how health professionals gave them hope by informing them that there is treatment and that they can be cured if they take their treatment properly. Those who had told to their families about their illness similarly received support and encouragement from them, which was of critical importance at this stage. A 46 years old male patient explained:

“It gives you hope to talk to the staff at the clinic. They tell you that you can live, that the drugs will help you. They say that we can come if there is a problem, this gives you hope.”

Another factor that most health professionals believed helped patients gain hope was the change that they saw on other patients, who were initially critically ill and later showed improvement. According to health professionals, that helped patients believe in the efficacy of treatment and hence gave them hope for themselves. A medical doctor states:

“I think many patients are encouraged to come because they see critically ill patients with co-infection who have improved. That gives them a lot of hope.”

Many patients indeed explained that seeing very sick patients who were coming supported improve and come to the clinic by themselves gave them hope, and encouraged

them with their treatments. After this initial period of loss of hope, most patients explained how an eagerness to survive was the driving force for their medication intake. Since prognosis was adversely perceived by patients in the presence of concomitant illness, many patients believed in the necessity to take drugs properly, in order to survive. A 50 years old female patient explained:

“You have to take what the doctors give you, you can not stop that. You can only survive if you take the drugs. Two diseases, it will kill you at once, your body can not support that. We are different from those who have TB only.”

All health professionals interviewed in this study believed that adherence to TB treatment in co-infected patients on concomitant treatment is not poorer than the adherence in HIV negative patients, as might be expected. These health professionals explained that, despite a pill burden that many patients are afraid of and other factors such as higher occurrence of side effects in these patients, their adhere to TB treatment was similar to HIV negative patients, in general. The most common reason given by health professionals was the eagerness by patients to survive, mainly a result of adverse perception of prognosis and severity of illness. They explained that many patients believed that TB might be very severe and might be lethal in their case because of the HIV infection, and hence usually adhere well to TB treatment, even after subjective symptomatic improvement.

Some health professionals also explained that most patients with TB co-infected with HIV had more severe symptoms at the beginning of treatment than the HIV negative ones, hence showed more eagerness to take drugs and see improvement. Health professionals also explained that, unlike some HIV negative patients, most co-infected patients did not tend to discontinue treatment once they improve because of fear of getting the initial severe symptoms again.

Another factor that both patients and health professionals pointed to was the importance to take TB treatment and show improvement, mainly improvement in weight, in order to avoid the suspicion of HIV infection by others. Some patients explained how weight gain

after few weeks of treatment for TB had helped them avoid the risk of being suspected of having HIV. One health professional, a clinical nurse, shared his experience:

“HIV positive patients, as compared to the HIV negatives, I think have a better adherence. Unless they have things that are out of control, for example economically, those who can not have food; they have an eagerness to survive. Even the feedbacks we get from them are pleasant. They tell us: I got better, I gained weight. Because they think that if you are positive, you will not get cured, you will not gain weight. When they gain weight, they are very happy. That is a good thing. The negatives, some of them, once they finish the intensive phase, they say: what if I stop now? The positives, once they start improving, they gain hope.”

Another factor also believed to encourage TB treatment intake was the fact that TB is known to be a curable disease, unlike HIV, as it has been known in the community for long, as illustrated in a quote from a medical doctor:

“Patients respect TB treatment, usually they default because of lack of supporter, or because they are forced to come every day. When you tell a patient that he has TB, he wants to start treatment, when you ask them to start ART, they want to wait. They have seen many patients get treated and survive TB in the community, but for the HIV, they are told that they will not be cured, so they say, why should I? You need more extensive counseling for the ART.”

#### **3.2.4. Perceived impacts of concomitant treatment**

##### **Pill burden:**

Most patients mentioned pill burden as being one of the major challenges of concomitant treatment. In addition to anti-TB drugs and ARV drugs, patients were also taking co-trimoxazole for PCP prophylaxis; and some in addition had to take drugs for other illnesses that they had. For many, the higher the number of pills, the bigger the damage it could cause to the body, and the higher the difficulty to tolerate the drugs. The amount and quality of food needed and the degree of possible side effects were also believed to be proportional to the drugs taken. Many worried, especially initially, about whether they would be able to tolerate so many pills. Patients used expressions such as “becoming a drug bag”, and “becoming a pharmacy” to describe the pill burden. A 36 years old male patient said:

“Swallowing so many drugs, it was very difficult. I was scared that it would harm my body. Drugs can harm you if they are too many, but I wanted to survive.”

According to some patients, the burden was also bringing mix up of drugs and also resulted in drugs being forgotten. The majority of health professionals also agree that the most important factor affecting patients during concomitant treatment is the pill burden, and think of it as the most important potential challenge against adherence. They explain that a frequent fear among patients when asked to take concomitant treatment is the pill burden. A medical doctor shared her experience:

“When they think about pill burden, they day, can I tolerate this, won’t this kill me? Taking many pills is perceived as lethal by some. Patients worry a lot about whether their body will be able to handle so many pills every day.”

Some patients also said that decreasing the number of drugs to be taken would facilitate medication intake.

In addition, patients also found it difficult to comply with the daily schedules of drug intake, which included swallowing TB drugs, followed by HIV drugs, and then cotrimoxazole, since it resulted in forgetfulness, as well as inconvenience with the daily routines. A female focus group participant explained:

“I had to take the TB drugs at 2 (8 a.m), the HIV drugs at 3 (9 a.m), and the bactrim at 7 (1 p.m.). Sometimes, there were other pills that they were giving me for other illnesses I had. That was very difficult, especially when you are working.”

### **Side effects:**

Side effects were experienced by many patients, mainly at the beginning of anti-TB treatment or upon initiation of concomitant treatment. Examples of side effects experienced by patients included: generalized body weakness, burning of the stomach, turning of the head, headache, bad dreams, rash, vomiting...The most common side effect patients had was burning of the stomach or gastritis. For many, stomach burning was believed to be due to excessive pills, aggravated with intake of inadequate or poor

quality meal. Generalized body weakness was also mentioned as a side effect by many patients, at times with inability to perform daily tasks.

A 46 years old male patient explains:

Q. Tell me about your experience taking the TB drugs and the HIV drugs?

It was very difficult. Very difficult. My body was weak; I could not keep my balance. Sometimes, everything was blurred, I lost my balance. It is a lot of drugs. It burns your stomach. Oh god! You burn! My stomach was out of use. The suffering! Don't think it is easy! It is not!"

Two of the patients interviewed had temporarily discontinued anti-TB drugs because of hepatotoxicity, and were subsequently reinitiated on treatment.

In addition to the actually experienced side effects, patients were also worried about side effects they hear about in the community. Some patients relied on the information circulating in the community about drug side effects. The commonest belief being that drugs can be dangerous and cause severe side effects if one is HIV positive, because the body is too weak to support drugs. Some had heard about relatives or neighbors who died due to drug side effects because their body was too weak due to HIV. ARV drugs in particular were thought of as being very toxic.

Many patients also believed that the drugs can “collide” (collision is what is referred to as drug-drug interaction in the biomedical term), and that they were worried about that when they started treatment. Some attributed their symptoms to the “collision” of the drugs. Drug collision is a common worry for patients in Ethiopia, and people usually ask about collision of drugs whenever offered two or more drugs together. Collision could be between drugs or between drugs and food.

One patient said he would prefer injections to drugs because it will not burn the stomach. Another person recommended the use of one pill including all drugs (fixed dose combination of ART were recently introduced, were not used by the patients in the study at the time).



Another common “side effect” mentioned by patients was a gain of appetite/excessive hunger, as discussed earlier, which was creating problems for those who could not afford to buy food.

Health professionals said that patients hear stories about side effects from other patients and also from the community at large and tend to get scared. A clinical nurse explains:

“...the problem that I also commonly hear, they (patients) hear people’s stories, like the side effects that other people treated had, and what if it turns my head, what if I vomit etc, they say. And some people also say that if a TB patient who is weak is started on ART, then he might die. There is a fear of death.”

According to many patients, health professionals had not warned them about potential side effects of TB drugs; nor did they know that these could be managed.

Worsening of symptoms was also one factor that was frustrating to some patients, mainly in the initial period of treatment. These patients recall feeling better before initiation of treatment than after starting the drugs. An example is a 40 years old female defaulter who discontinued her TB drugs and continued with the ARV drugs. She said she is happy and made the right decision because her symptoms (weakness, loss of appetite, turning of the head) were worse than before treatment and that they improved after she stopped the TB drugs and that she was now able to work.

#### **Lack of food:**

Lack of food was a common problem that patients mentioned. The majority of patients in the study believed that high protein diet such as milk, eggs, were needed while on TB treatment, and, for some even more so while on concomitant ART treatment. Many had been informed by health professionals to consume such diets upon initiation of treatment, but many also knew about the need for such diet from before, from what they heard in the community, where it is believed that milk, eggs...are important for someone with TB. Not being able to afford good food therefore created a problem for some patients who believed that the drugs would harm their body because of this. Others also mentioned that

it would be better not to take the drugs than to take them on an empty stomach. A 36 years old male patient explains:

“When you have two diseases, you need good food. Otherwise, it will harm your body. It is better not to take the drugs. The drugs alone, it might kill you.”

Many patients also experienced a gain in appetite some time after initiation of TB treatment, and were unable to get food to satisfy their appetite. That resulted in a fear of having the body harmed because food was believed to be important to avoid damage to the stomach when one uses so many pills; and the lack of food was also thought to affect the healing process, the cure from the TB.

Health professionals recognized the problem of food as being common, especially with the gain in appetite related to improvement. A 32 years old clinical nurse explained:

“Q. How about the problem of food among patients?

That is a very serious problem for many of our patients. They almost want to kill us wanting help. They come here asking for help from NGOs. They say that especially TB drugs increase appetite. They feel hungry after they start feeling well a bit, and food becomes a problem.”

Dietary advises regarding consumption of high protein diet were very often given by health professionals; patients being told to consume foods such as milk and eggs. In addition, some health professionals also explained that the media also emphasizes the use of adequate food in the presence of HIV infection, which makes patients give excessive attention to the problem of lack of food, and also to the quality of food consumed. For two of the defaulters in this study, lack of food was a major factor in their decision to stop treatment.

Patients who had dietary restrictions because of the ART drugs that they take such as for example efavirenz with which consumption of high fat diet is contraindicated faced even more dilemmas. A 36 years old patient who also had to temporarily discontinue treatment because of hepatotoxicity explains the challenges he faced.

“TB needs food with fat, and liver does not want that, it is a tragedy for us, because you do not know what to do. Even the life prolonging drug does not want fatty food. That is if you can afford fatty meals anyways. ”

Many patients said that provision of food by the health center or NGOs would facilitate medication intake, when asked about what could be done to facilitate medication intake for patients in their situation.

### **3.2.5. The role of the health personnel**

The majority of patients in the study were happy about the way the health professionals received them at the health centers, many were grateful for the affection that they received from health professionals. Many were encouraged to come for treatment because health professionals were receiving them with a “good face”, and were encouraging them to finish their treatment. A 20 years old female patient said:

“They (health professionals) were very good to me. They are like friends, did you not see? Since my head was not good, they were giving me the drugs in a certain way, in a bag, so that I know which drug to take when, they translated it in Amharic for me. They gave me a watch, they helped me a lot. They were like relatives. I have no words to thank them. I am standing today because of them. They told me what drugs to take at what time.”

The support was mainly important in the initial months of treatment, when loss of hope and difficulties to tolerate drugs made medication intake difficult for patients. For many, support from health professionals and counseling they received were major factors that assisted them with their decision to embark on treatment.

But, when asked about whether they received information about their illnesses, or about the drugs and potential side effects, many patients replied that they did not get any information; except the few who had asked the health professionals the information they needed. Those who asked questions tended to be more educated in general. A male focus group participant said:

“Someone might be kind, that is not because they always give me drugs, they should also ask me what did it cause on you, is it good, did it cause any harm, what can we do for you? They have to say this. I come, they see my card, I get my drugs, and I go. That’s all. Someone might be good naturally, but when I see from profession, it is less than I expected.”

Some felt the need to ask questions about their treatment and the drug but did not do so because they believed the health professionals did not have the time to reply to everyone’s question.

Most patients explained that they were given information about factors such as the need to consume high protein diet, the need to abstain from sex, alcohol and smoking; they were also told that it is important to finish treatment. But many patients were not told about the relationship between TB and HIV, about why they needed TB treatment for eight months, about the side effects that the drugs can have, and about concomitant therapy since many were worried about “drug collision” during concomitant treatment.

The information received had at times been misunderstood by some patients, whom, for instance, were taking sex as a route of transmission of TB because all they were told by the health professional was that they should abstain from sex while on treatment. In addition, not knowing about possible drug side effects and the fact that they could be managed adversely affected treatment of patients who thought that stopping treatment would be the solution to their problem. Some patients were also taking drugs for eight months without understanding the need for this long treatment. Much of the knowledge that patients have came from the community, from other patients at the health centers and mainly from the media.

Health professionals agree that patient-provider relationship is very important in the treatment of patients. They also explain that lack of time with high burden at the clinics has made it difficult for them to spend adequate time with their patients and provide all the necessary information. Most also believe that adherence counseling is critical for patients, mainly for co-infected patients on concomitant treatment because of dual long term treatment, and that patients should be evaluated for their drug intake every time they

come for a visit, but that it has been difficult to do so because of the time constraints. A clinical nurse said:

“What we do is not enough. The counseling should be done every time they come for treatment. Sometimes, we just give them their drug and send them home. You do not even know if they are taking the drugs the right way.”

During my interviews, I found patients who told me that health professionals informed them they had *bird* and initiated them on TB treatment. I raised the issue to health professionals and I found two kinds of explanations. Some said that some health professionals were telling to patients that they have *bird* because they themselves believed it could be a cause of illness or because it is easy for patients to understand. Another health professional, a medical doctor from one of the clinics, had another opinion:

“You know what happens? When patients talk about *bird* to physicians, physicians do not respond. They simply say, ok, we will give you drugs, and you will improve. Then, they think you agree with the *bird* theory. That is because there is no time to explain.”

Many health professionals also mentioned the media as a good channel of communication for patients that can be used to give health education on TB as well as on co-infection. All said that TB has been neglected in general in health education campaigns and in the media as compared to the increased attention that HIV has received. One of the observations I myself made during my fieldwork was that many of the posters used in the clinics were posters about HIV, even the ones posted outside the TB offices. Information pamphlets were also available in the HIV clinics, with information both about the illness and about ARV treatment, but were non existent in the TB clinics. The knowledge that participants in the study had about TB as compared to HIV was also reflective of this; many patients having had the chance to learn about HIV from the media, but also from the community, where awareness about HIV, I believe, is higher than that of TB, in view of the information available.

Health professionals gave examples such as the media's role in promoting bed nets for malaria, after which a high use of bed nets and a decrease in malaria incidence were noted. But many health professionals also said that the information provided on the media should be made clear, understandable by the general population and more sensitive; and explained that information provided by the media has at times been the source of misunderstandings and that the media is partly responsible for the stigma that is present against HIV.

### **3.2.6. Coming to the clinic every day: the challenges of DOT**

The absolute majority of the patients found DOT with daily supervision of treatment for the first two months a very difficult task to accomplish, as well as an expensive routine. The initial phase of treatment during which daily supervision is made was the phase when many patients were ill and weak, which meant that they often had to come to the clinic accompanied by their families. That made patients feel guilty because they were putting pressure on their close ones who were already struggling to make their living. In addition to physical weakness, transport costs were also a problem for many patients. In addition to the daily visits to the TB clinic, patient also had to attend the HIV clinics on a twice monthly or on a monthly basis and at times more frequently. A 35 years old female patient shared her experience with DOT.

“Q.What was it like coming to the clinic every day?

It is very difficult. TB, you know, it is a very difficult disease. You have no energy; even your dreams are bad. The transport money, it is too much, I finished a lot of money. People helped me, thanks god. I had to come every day for injections. I tell you the truth, there was a time when I had to sell my jewellery: my rings, my necklace, everything. I had to run here without even eating breakfast.”

Few patients also explained that they were taking the drugs for their own good, and therefore needed to be given the drugs. A male focus group participant said:

“I come for treatment for myself. As long as it is for myself, I do not have to come every day. I am the one who will be harmed; I am the one trying to survive, they can give me my drugs.”

A health professional shared his experience with patients who felt that they were treated like kids and were thought of as being non- knowledgeable by being given the drugs daily at the health centers:

“There are some (patients) who say: swallow, don’t swallow, do you think I am a kid? I know for myself. Do you think you are the only ones with knowledge? Some even throw the drugs at us and leave.”

Another concern for some patients was that coming to the clinic every morning was exposing them to the cold and aggravating their cough.

All health professionals agreed that DOT with daily supervision is a difficult task for most of their patients. Most believed that DOT is too rigid, and some stated that something has to be done to modify the daily schedule into a better schedule for patients, like a once weekly or twice monthly schedule. Some were giving drugs for patients for 3-4 days when these reported a strong argument for not being able to come to the clinic every day. A medical doctor explained:

“I know there is a problem with individualizing treatment, but, if there is a committed health worker, it can be good. As long as the reason for DOT is properly told and as long as side effects etc. are properly monitored every time the patient comes, and if they assess what happened when the patient did not come, then I think it is ok to have some flexibility. We are doing this with ART where they say adherence should be more than 95%, right? Why not trust them with anti-TB as well? Asking a patient to come every day, it is a punishment.”

Others were very strict with DOT and said that the patient has to come every day if he is to achieve cure, and said that they were worried about drug resistance. They expressed past experiences where flexibility had resulted in improper drug intake. A clinical nurse explained:

“I have some bad experience. I gave a patient drug for a few days because he was telling me he can not come. He divided the drugs and started swallowing them BID (twice a day). I had that experience.”

It was many patients’ opinion that drugs need to be given to families at least when the patient is too ill to come. Health professionals had a divided opinion on this issue as well. Some said that they would give drugs to relatives if the patient is very sick. Others said it

is very important as well as a guideline from the NTLCP that the drugs have to be swallowed in front of the health professional and showed more rigidity in this regard.

Another challenge faced by some patients in the health center was the necessity to bring one person responsible for their treatment. The national guideline says that, before starting anti-TB treatment, every patient has to bring one person who will be responsible for his/her treatment and who might be contacted by the health system if the patient does not come for treatment. Some patients chose not to reveal their diagnosis of TB for anyone for fear of being stigmatized, and hence found it difficult to find someone responsible for their treatment. In addition, according to some health professionals, the necessity of being treated within the health centers in their neighborhood was a problem for some patients, who did not want to be seen by people from their neighborhood. A clinical nurse shared her experience:

“I also had a patient who was cyanosed, critical, and he survived by miracle. He said: Let me die if you give me treatment in my sub city, because he did not want to be seen by neighbors.”

Health professionals also faced the dilemma of accepting patients without I.D. cards, since the rule is that all patients coming to the health centers for TB treatment should have an ID card. A health officer shared her experience:

“Once I accepted two patients with no ID card because they said they could not get one. One finished, the other disappeared. I didn’t have anything to find him. The reason for the ID card is to have an address to trace them when they default. It is such patients on the street with no address who are the reasons for increasing default.”

Another major challenge associated with DOT was the impact on patients’ income because of the obligation to attend the clinic every day; which was either not suitable with their working schedule, mainly for those who had no fixed jobs and had to go out early in the morning and look for a job; or was creating problem with employers for those with fixed jobs, mainly those who did not want to convey their diagnosis. That created a major stress on some patients, for whom TB treatment for the first two months equated



with loss of income. Most patients thought that the waiting time at the TB clinics is reasonable, although some patients reported long waiting hours after being told that they had to wait for drugs to arrive or because the health professionals were not there.

### **3.2.7. Collaboration between TB and HIV clinics**

One of the recommendations in the WHO's policy for collaborative TB/HIV activities is that "TB and HIV programs should ensure a continuum of care and support for people living with HIV, during and after TB treatment" (6).

In two of the health centers I worked in, TB and HIV clinics were co-located. In the third clinic, construction of co-located TB and HIV clinics was finished as I was about to complete my field work and work was initiated there. But, although physically co-located, the two clinics were operating independently. A patient was managed as a TB patient in the TB clinics and as an HIV patient in the HIV clinics. In the TB clinics, the health workers were often times not aware of which patients are co-infected and on concomitant treatment, unless they see the patients and remember their HIV status since they were the ones who screened most of them; or unless they referred to the PICT register. In one of the health centers, information on HIV status and on whether the patient was on ART or not was filled out in the remarks column of the TB register. Again, two weeks before I was about to finish my field work, a new TB register was introduced, and in this new register, in addition to the information present on the old register, other columns were added which show whether the patient was tested for HIV, his HIV status, and whether s/he was initiated on ART or not, and when the ART was initiated.

Most of the health professionals also underlined the fact that collaboration has been poor. Some said that the staff in both clinics should be trained in both TB and HIV management to be able to respond to patients' needs. In addition, health professionals also worried that the information provided at the two clinics might sometimes conflict, and create confusion among patients. A clinical nurse explained:

“The problem is, there is TB, there is HIV, and those of us at the TB and at the ART clinic, we are not getting along well. We might have a common patient, and if the information we give is different, for example if we have a patient with low CD4, with extra pulmonary TB, and if I say he should start ART in two weeks and if they tell him to come back in two months, whom should he trust?”

Some health professionals also expressed concern that patients might get lost from either clinic without health professionals in the other clinic knowing about it. A clinical nurse in the TB clinic said:

“Sometimes, the patient comes from the ART clinic, when I ask him here if he is having a follow up, he might say yes without going there, so patients might get lost like that. The collaboration is not good.”

In addition to provision of training in both TB and HIV management for staff in the TB and HIV clinics, health professionals also suggested that regular joint meetings should be arranged to discuss matters related to common patients.

One health professional expressed concern that, although the collaboration is important, it could also potentially increase the stigma against TB because of the association with HIV. She explained that it could adversely affect mainly those patients who only have TB and come for treatment at the TB clinics, and explained that collaboration should be done with caution.

Some patients similarly felt that the collaboration between the two clinics is weak, and said that more should be done to arrange patient appointments on similar days at the two clinics, to avoid repeated visits at the clinic to take anti-TB and ART medications. A male focus group participant shared his experience whereby a drug that should have been changed because of his anti-TB treatment was not changed at the HIV clinic since his intake of anti-TB was temporarily forgotten at the HIV clinic.

### **3.2.8. The influence of stigma**

The majority of patients said that TB would predispose to stigma. For most, stigma was mainly due to the fact that people associated TB with HIV. This resulted in many patients

hiding their diagnosis of TB or only disclosing it to selected people, mostly close families. A male focus group participant told:

“Before, I knew a lot of people with TB who did not have HIV. But now, if you say you have TB, people will take it to HIV. Me, even when I take these TB drugs, I don’t tell to anyone.”

Fear of stigma not only lead to patients not telling about their illnesses but also made seeking TB treatment in their catchments areas difficult as mentioned earlier, for fear of being identified by neighbors there. Many health professionals had experienced that with their patients. Since the regulations of the NTLCP are that a patient should be treated for TB within his/her catchment area, health professionals face problems with patients wanting to be treated in their clinics without belonging to the catchment area( recently, similar problems have lead the HIV clinics to accept patients coming from any area to be started on ART). A 36 years old male patient told:

“I don’t want neighbors to see me here (TB clinic). So, if I have an appointment in the morning, I hide and I come late, and I lie to the nurses here; I tell them that I had something else to do. Everyone comes early in the morning, so I come at around 5 hour (11 a.m.). One day, I saw this girl from my neighborhood here; I was sitting outside and waiting. I wished the earth would open and swallow me. I know she would spread the gossip. I tried to hide behind the man sitting next to me. I don’t think she saw me.”

Patients said that HIV associated stigma is what they feared the most. Many had seen other HIV patients suffering from stigma in their communities, and said the same might happen to them. Some shared their personal experiences of HIV related stigma which included being pointed at in their neighborhoods, neighbors gossiping about their illness behind their backs, exclusion from social events, and mainly events that needed their active participation such as group meal preparations for funerals. Many patients believed that, although both TB and HIV are stigmatized, there is more stigma attached to HIV. Many also said that HIV related stigma has improved from before; an opinion also shared by all health professionals, many of whom believed that is mainly because of the introduction of ART making the community believe of HIV as a chronic manageable illness, and not a lethal untreatable illness like before. Some patients said that they were

hiding the HIV, and not the TB. A health officer shared her experience telling that some patients had asked her to mention only the TB and not the HIV on their medical certificates, which they usually bring to their employers.

Many patients said that, in addition to the cough, losing weight was the factor that made them vulnerable to stigma the most, because that indicated that they also have HIV; many patients themselves believed that a patient with TB only has a higher weight and is “stronger” than them. Gaining weight quickly was therefore important; to avoid suspicion of HIV, and patients who managed to gain weight early would be very satisfied and encouraged to continue treatment, according to many health professionals. In Ethiopia, weight gain is seen as a sign of health, and someone who has gained weight would be complimented and would be told that he looks healthy. Weight loss is often perceived as a sign of illness, and excessive weight loss in a patient who is sick is frequently associated with HIV infection, since the advent of the HIV epidemic.

Some patients said that the media was responsible for the fact that people were automatically associating TB and HIV. Health professionals also share this opinion.

A clinical nurse explained:

“You know, the people they interview on the media usually say: I had TB and I was told I am (HIV) positive. So for those who listen to it that would mean: ok, if there is TB, there is HIV.”

Those patients who knew that TB was transmitted to others through the respiratory route also said that people were staying away from them because they were afraid they would catch TB from them. One patient reported leaving her sister’s house and moving out of Addis-Abeba because the people who were renting the house to her sister were afraid of her cough and told her sister that they were afraid to get diseased as well. Another patient explained that she had lost her business and gone into absolute poverty after customers buying *tella* (traditional alcoholic drink) that she sold to make her living stopped coming for fear of catching her illness, since she had been coughing for long. Some patients also

had experiences with families isolating their eating and drinking utensils, as well as not allowing them to do works at home, such as cooking. Others reported not being invited by neighbors for coffee, people not visiting them anymore, and people “changing” on them.

### **3.2.9. Social support**

Social support was a very important factor affecting many patients’ treatment. In this study, as mentioned earlier, most of the participants told about their illnesses, both TB and HIV, only to close families. Few had informed others about their diagnosis of TB but had hidden their HIV status, for fear of being stigmatized. The support of close families was therefore the only available support for most patients; and was found to be critically important for many. Many had been seriously ill when initiated on treatment and had been in need of someone to accompany them for treatment. Families also provided food and transportation money for patients, since some had no income and others had to stop working for some time. Families were also a source of encouragement and comfort when patients had lost hope. Many said that they were able to take their drugs and survive because of the support that they received from their families. A female focus group participant explained:

“My family members supported me a lot. They encouraged me. After the TB, when they found the HIV, I wanted to die. I did not want to live. But my families, especially my brothers and sisters, they said: you are not the only one. Look, many people have this. And we are in a good period, you can get treated for your TB and your HIV and live a life like anyone else. It is because of them that I am alive today.”

Health professionals also believed that patients who had family support and come to the clinics accompanied are usually the ones who successfully complete their treatment, and explained that having some form of social support was vital for adherence.

But getting support, mainly financial, made some patients think about themselves as a “burden” to their family; one of the defaulters in the study said that one of the reasons why he discontinued treatment was that he did not want to be a burden to his families

who had to provide transportation money during DOT as well as the food he needed to tolerate treatment. A 20 years old female patient who had to give up her work as a commercial sex worker after being diagnosed with TB then HIV similarly explained:

“There are many problems in one person’s life. You do not have transport money. A sick person has many expenses. You do not have any money on you. They should give you (TB drugs) for one month. To ask money from your family, it is a burden. I feel sad, because I was the one giving money to my families. Now, I ask for money, even for transport money. That damages you.”

Some patients appreciated the help of local NGOs providing them with cereals, and at times transport money, while others complained about not receiving enough support from these NGOs or that the support had been delayed. According to health professionals, local NGOs have been providing food and also transport money for treatment for HIV patients. Some also provided home treatment supporters for patients who had no family support; others provided money for patients to start small scale businesses to support themselves. Although the support was found to be important by health professionals, it had also resulted in high expectations from patients who needed health professionals to refer them to such NGOs, even when no specific contact existed with the NGOs and the health centers.

### **3.2.10. The economic burden**

This has been already discussed in large in the previous sections, and will be briefly presented here. Costs related to the illnesses, both TB and HIV were both direct and indirect. Many patients had had long periods of illness and had consulted different health facilities, mainly private, before the start of their treatment. Many had been supported financially by their families starting from this initial phase. A 50 years old female patient who had been ill repeatedly before getting diagnosed with TB and HIV explained:

“I used to rent a place and work, and when I was working, I got sick. I finished all the money I had saved on the hospitals. I was going to private clinics and getting treated and treated and treated.”

In addition to costs related to treatment, some patients had to stop working because of severe illness. That meant that they needed financial support from families for their treatment costs as well as daily costs. Although TB and HIV treatments are provided for free for these patients, transport costs, especially during daily treatment, were too expensive for many patients. A 30 years old male patient explained:

“It is difficult. You have to come every day. We come here in the morning and take our drugs. And you also have to come for the life prolonging drugs. The transportation money, it is not easy for some of us. Sometimes, I walk, if it is not too much sun. But sometimes, you get tired, so you have to take the taxi. It is not little money.”

As discussed earlier, the routines of DOT had cost some patients their jobs and compromised others’ because of the necessity to be present to the clinic every day for two months. This made patients require support from others which in turn resulted in a feeling of guilt; because of the burden they felt they imposed on their families.

In addition, the need for high protein food also imposed problem for some of those who could not afford it, since they believed that they needed that type of food to improve from the TB and since many also believed in the importance of gaining weight as a sign of improvement and as a protection against suspicion of HIV and resultant stigmatization.

### **3.2.11. Right timing of ART treatment**

In general, the recommendation is that, in a co-infected patient, the priority is given to the treatment of TB no matter how advanced the HIV is and to start ART according to clinical conditions and CD4 counts; and WHO’s recommendation on the initiation of ART in co-infected patients is what is used in the clinics. There is room for individualization in this case. Those patients already on ART upon diagnosis of TB are continued with their ART and initiated on anti-TB treatment.

Many patients in this study had been initiated on ART upon completion of the intensive phase, some were initiated in the intensive phase, and few were already on ART when anti-TB was initiated. In general, patients faced a dilemma when confronted with the possibility of starting concomitant treatment versus delaying ART. Many were worried

about pill burden and about whether their body was ready to tolerate the drugs, in addition, for some, other problems such as the lack of food...existed; but patients were also concerned about the risks of delaying ART. But most who were told by health professionals that ART will be delayed until the end of the intensive phase said they took the recommendation positively, since their fear and doubts of starting concomitant treatment immediately were for them confirmed by health professionals usually telling them that it is better to delay the ART. Some also believed that their body would “adapt” to the TB drugs with time, and it will make it easier for them to tolerate the ART.

According to health professionals, some patients are eager to start their ART after initiation of anti-TB but that many also fear factors such as pill burden...and want to delay treatment. A medical doctor explained:

“Some patients do not agree to start the ART before they finish the anti-TB, for fear of pill burden, and you can not force them, even when you know that they need it. I’m talking about patients with very low CD4 counts, stage IV patients.”

Health professionals said that adherence counseling is provided and the patient’s readiness to start concomitant treatment assessed before initiating the ART. Some health professionals also said that they were able to see the adherence to cotrimoxazole preventive therapy during this time and have some assessment of what the adherence would be like in these patients.

Three of the patients who defaulted treatment in this study said that initiation of ART in the intensive phase of their TB treatment had been too difficult, and that they were unable to tolerate treatment, and claimed that delaying the ART would have been better in their cases. A 36 years old male defaulter who had discontinued both anti-TB and ART drugs explained:

“It is better to take one drug and then the other drug. Your stomach can tolerate it. Your body can tolerate it. Together, it is too much. That is why I stopped my drugs.”



### **3.2.12. The impact of gender**

It was quite difficult to assess the impact of gender on treatment in patients because questions regarding this subject were usually poorly understood by patients, most probably because they did not think of gender as a factor that affects treatment.

Some health professionals said that, in general, women tend to adhere better to TB treatment than males, although females usually tend to be more delayed in seeking treatment than males. The reasons given included the ability of women to tolerate stress more, an opinion shared by two health professionals. A clinical nurse explained:

“Females follow treatment better.

Q. Why do you think that is the case?

I think females feel more responsible. And they tolerate problems more. Often, men do not want much stress. Even when there is discordant (HIV) result, if the man is negative, they usually disappear. When the female is negative, she is with him till the end. I think females have the ability to go face to face with problems.”

One difference that was apparent in my data was that there was a difference in what worried males and females more when it came to consequences associated with TB treatment, together with ART. For men, what was worrisome was the fact that either the illness or the necessity to constantly attend treatment would affect their jobs, and hence would affect their income; and this affects them as well as families who were usually dependent on them. For females, the biggest worry was what would happen to their siblings if they were not able to survive their illness. Females also worried more about what the community or neighbors thought about their illnesses, and reported incidences like not being invited by neighbors for coffee as being a serious problem associated with their illness; whereas males tended to be less worried about such incidences, and usually did not tell their illnesses and claimed that they decided to live their own life. Hence, it would seem like males usually confronted the challenge of having to make a choice between treatment and their income; and might be forced to discontinue treatment if the loss of income would appear to have more immediate consequences than the illness itself, mainly once they get some symptomatic relief. Females also have big burdens on their shoulders, and, even though more females were unemployed than men, the daily routines at home were also very demanding. But it seemed like females managed to make time for

their treatment while at the same time managing their daily routines. Showing quick improvement might also be very important to women in order to be able to have their place in their social sphere and avoid stigma, since socializing with neighbors and attending ceremonies such as coffee ceremonies were very important to women.

### **3.2.13. Alternative treatments:**

Use of traditional medicine was not a common practice among participants in this study. Many patients simply preferred modern treatment over traditional medicine, and others explained that the reason for not consulting traditional healers was related to the fact that they did not trust traditional healers present currently; they believed that “good” traditional healers were not here anymore, and doubted that the now available traditional healers had the right plants for treatment. A real traditional healer would be an old man who has inherited the practice from his father and would in turn train his male siblings to do so. Thus, according to some participants, there was a belief that those elder traditional healers are no longer present and now, some people are just trying to call themselves traditional healers, and thus, they were unable to trust them. A 36 years old male patient said:

“These days, who will go to the traditional healers? Who will trust them? How do you know what plants they give you? I do not go to the traditional healers.”

Other patients said that traditional medicine is good for some illnesses such as *almaz balechira* (local term for herpes zoster), for which they had consulted a traditional healer but said that modern treatment is better in the case of TB. Health professionals also believed that the use of traditional medicine for TB was not a common practice among their patients from their experience, but said that patients consulted traditional healers for illnesses like *almaz balechira*, as was also mentioned by patients. *Almaz balechira* (herpes zoster) is a common illness in HIV positive individuals and is due to reactivation of the varicella zoster virus secondary to immunosuppression. There is a very common belief in the community that it is due to an insect bite and the best treatment is believed to be traditional medicine, and a famous traditional healer in Addis-Abeba, Ato Mammo, is

particularly known for treating this illness; in recent times, the association between herpes zoster and HIV is becoming known to the community, which many patients in this study were also aware of.

Many patients had used home remedies such as warm drinks and at times herbs, hoping that the cough, which was frequently thought to be due to *bird*, would subside. Patients eventually consulted health services, at times visiting several private clinics before being diagnosed with TB and coming to the health centers or coming to the health centers because they could not afford the private clinics any more.

Some patients had also taken *tsebel*, which is holy water that is commonly used by followers of the Orthodox Church, sometimes also by people who are not followers of the orthodox religion. Holy water can be collected from the churches and taken at home but can also be used in the churches and given by priests, with different durations of “healing”, most frequently 7, 14 or 21 days. All of the patients who used holy water in this study used it together with their anti-TB and ARV drugs; except one defaulter who had given up all his treatments and gone for holy water, hoping to get cure. Another patient was contemplating giving up her ART and go for holy water. In the past, it used to be more common that one either takes drugs or *tsebel* and not both. With the advent of the HIV epidemic, and the introduction of ART, priests in the Orthodox Church are preaching concomitant intake of *tsebel* and drugs, since many patients were abandoning their ART treatment and going for holy water.

Health professional also confirmed that, although few patients abandon treatment to go for holy water, more and more patients are now using *tsebel* and drugs together. They also explain that more patients abandon *tsebel* over ART than those who abandon it over anti-TB. That can be explained by how the disease causations are understood by patients. In this study, some patients referred to HIV as being a disease of Satan that can not be cured, even with drug intake. Others thought of HIV as a punishment from god for sinful behavior. Hence, religious healing such as the use of *tsebel* might be considered more important for HIV than for TB for some patients. Few patients also thought of having

both TB and HIV as being a punishment from god, and took both their drugs and *tsebel* together. A 46 years old male patient said:

“Two diseases at the same time! I felt cursed! I said: God, why? Why two diseases for me? (He stops conversation for a while) But you can’t change God’s will, so I had to accept it. What was expected from me was to take my drugs properly; the rest is up to god.”

Another patient, 30 years old male, similarly said:

“I said, why do two diseases come on me? I am sad that I am like a bad person. Given two diseases. I am not a bad person; you can ask anyone about me, they will not tell you I am a bad person.”

Few patients also said that *tsebel* is not good for TB because it is cold and can worsen the cough, but said that it is good for HIV.

“...*samba* (TB) doesn’t like cold. *Tsebel* is cold. You should use warm things. You can’t use *tsebel* when your lung is diseased.”

### **3.2.14. Cases**

Next are two cases I selected because I believed they show the interplay of factors involved in the experiences of drug intake of patients. The first case involves a patient who defaulted treatment, whereas the second case involves a patient with successful treatment completion.

#### **Case 1**

This is a story of a 57 year old ex- soldier currently earning his living by repairing umbrellas. He has an irregular income, which he can not estimate, and he says that he just waits for work and for people to come. He can write and read, but has no formal education. He is divorced, and has two children who live in a neighboring country with their mother. When he starts coughing, he ignores his symptoms for a while and continues to work, until people who noticed his non stopping cough tell him to consult a treatment center. He does so after a while, and is provided free treatment at the health center, where, after chest x-ray and sputum exams are conducted, he got diagnosed with TB. At the same time, the health professionals ask him whether he would volunteer to have an HIV test, which he agrees to, and he is told that he also has HIV. He was then

started on anti-TB and, few days later (he does not remember exactly how many days), he was told that he needs to start ARV drugs, and is started on those.

When I ask him about what he thinks causes TB, he tells me that it comes from another person through respiration, because the health professionals had told him to cover his mouth not to transmit the disease to others. He says that HIV can be transmitted sexually, as well as through razors and through blood. But he also believes that TB turns into HIV, and insisted he heard that information on the radio.

He takes his medications for some time, but starts experiencing very unusual feelings, such as hallucinations, feelings of upset, and he was unable to sleep at night. (Efavirenz, an ARV drug that is used in the health centers, and which he also received has central nervous system side effects such as confusion, abnormal thinking, impaired concentration, abnormal dreams, insomnia, and hallucinations). In addition, he experiences hunger, but was not able to afford the food he needs. He recalls his experience at the time by telling me that the medications made him very upset; that he would ask himself what type of drug it is that would give such symptoms; and that, although he was getting hungry, life was too expensive for him to get the food he needed. He decides to continue with his drugs, thinking about the situation and his health; “I wanted to live, so I continued the drugs”, he says. He receives support from health professionals who encourage him to take his drugs and even provide him with left over foods. His families are not around and he chose not to tell about his illnesses to anyone, so health professionals are the major source of support for him; he sometimes gets left over food from people on the street. He says that health professionals were more supportive than he expected.

When I ask him about whether he believed TB is curable, and how the presence of HIV affects that, he tells me that if the TB had changed into HIV, then the body is weaker, and because of his age and because of his “bad life” also, it might be difficult for him to get cured but not impossible; but says that he has seen people who came supported by others improve and come for treatment by themselves.

Despite the difficulties with side effects and lack of food, he continues his treatments for three months until he decides to abandon all treatments. He elaborates on his experience and his decision to stop treatment by telling me that he started the drugs with few days difference hoping to save himself from suffering but that he was unable to know which drug gave him the problems and that he lost energy, and was unable to get food although health professionals had advised him not to take medications without taking food. He tells me he was eating beans soaked in water until he abandoned his medications. He says that the nightmares were frequent and that he had an urge to run away at night and that, since he had no one beside him, he got scared and stopped all drugs.

Although very grateful for the support he received from health professionals, he expresses his frustration about being compared to other patients by them. He tells me that it is not right to compare him with someone with good life and give him the same advises. He says that, if his life was full, he would also have taken the drugs properly. He says that he does not want to be a burden to anyone, and that he has made his decision to stop his treatments.

He also tells me that, provision of food would facilitate medication intake for people in his situation, and also says that taking one drug followed by another can lead to forgetfulness and thinks that health professionals should do something about that. The other comment he gave was that he believed that in his case, he should have been given the TB drugs first, since those are only taken for some time only, and then the HIV drugs, and not both together, like he was offered. When I ask him whether the health professionals had explained the need for ART and asked his opinion on starting ART, he tells me that he was told that the illness had harmed his inside and that he needed the drugs and agreed to it because he wanted to survive.

## Case 2

This case involves a 36 years old male patient, single, with secondary education. He works as a broker, a private job that is flexible in terms of time schedule, and which provides him with a fair income.

He has been treated for TB before; and relapsed shortly after completing his TB treatment. He had taken six weeks of anti-TB treatment for the second time when I interviewed him. The first time, he was started on ART two months after he started his anti-TB treatment. He recalls being sick for a long time, with body weakness, pain at multiple joints and swelling of the legs followed by cough. He then went to a private clinic where he was told that he needed to be tested for HIV, and, in addition, sputum exam and x-ray were taken. The HIV test became positive, and he was also diagnosed with TB and was told that his lungs were damaged and that he also had water around the lungs. He explains that this period was very difficult for him and that he even contemplated committing suicide, he says that life was dark at the time.

He says that he had been exposed to *bird* and that it was the reason why he got TB, but says that, after he came to the clinic, he was informed that HIV predisposed him to TB even more. When I ask him why HIV predisposes to TB, he explains that getting one disease harms the body and makes one more liable to get another disease.

He shares his experience of concomitant drug intake the first time he received TB treatment by telling me that the pills were burning his stomach and were too many and that he decided to discontinue the bactrim (co-trimoxazole). When I ask him why he chose to stop bactrim, he tells me that some patients stop bactrim and nothing happens and says that even the doctors are not so strict with that drug. When I ask him: How about the anti-TB? He replies that he was told by the nurse that TB will kill him before HIV does if he does not take the drugs properly.

He also tells me that he was receiving injections (streptomycin) for the first two months which were painful because his body was harmed by the cold. He is then diagnosed with a problem on the liver after blood tests are conducted, and he temporarily discontinues his drugs which are subsequently restarted. He explains that his illnesses (TB and HIV) need good food, and that he tried to consume those during treatment, although the restrictions of fat because of his ART drug and also because of his liver problems made it difficult to take high fat foods. He explains the importance of gaining weight and

showing improvement in order to avoid stigma by telling me that these days, when someone starts losing weight and his face starts to change, everyone suspects that he has HIV. He says that he only told about his illnesses to his close families, and says that, if he tells to others, everyone will be pointing fingers at him. He says that he was lucky because he quickly gained weight after starting his anti-TB treatment, and that people thought “he was ok”.

He also tells me, even though he was afraid that the pills will harm his body because they were too many, and even though he was experiencing side effects, he continued his drugs because he wanted to live; and that he was told by the health professional that with HIV, TB will kill him if he doesn’t take his drugs.

When I ask him what else encouraged him to finish treatment, he explains that the help from health professionals was very important, and says that if it wasn’t for them, he might have been dead by now; and he appreciates that they were giving him answers to his questions. He also says that it is difficult to come to the clinic every day for the first two months. He says that it is mainly difficult for patients who are very sick, because the *bird* is forceful in the morning and can harm them. He also believes that it might be difficult for those who have regular work, because they might be late for work, but, in his case, his work schedule is flexible. He also says that the waiting time is not so long in the clinics.

When I ask him why he thinks he got TB again, he tells me that, the last time, he has taken his medications properly, that he did not skip even a single dose, and says that he thinks he got TB again because he was hit by *bird* again. He believes that TB is curable, even in the presence of HIV, although it might be more difficult. He says that mainly for those who are weak, who come supported by relatives, it might be more difficult to get cured and says he is lucky, because he is not like the others, because his body is “full”.

When I ask him to compare his TB medication intake this time and the first time, he tells me that, since his body has now adapted to the HIV treatment, it is easier for him to



tolerate the drugs this time but he says that drugs always collide and fears that he might have problems like the first time (liver problem).

These cases shows how a number of factors act as barriers and facilitators of treatment adherence in one patient and how the end result is just a matter of which factors predominate and are given importance by the patient to tilt the decision in a certain direction.

Fig .2 presents a summary of the findings.

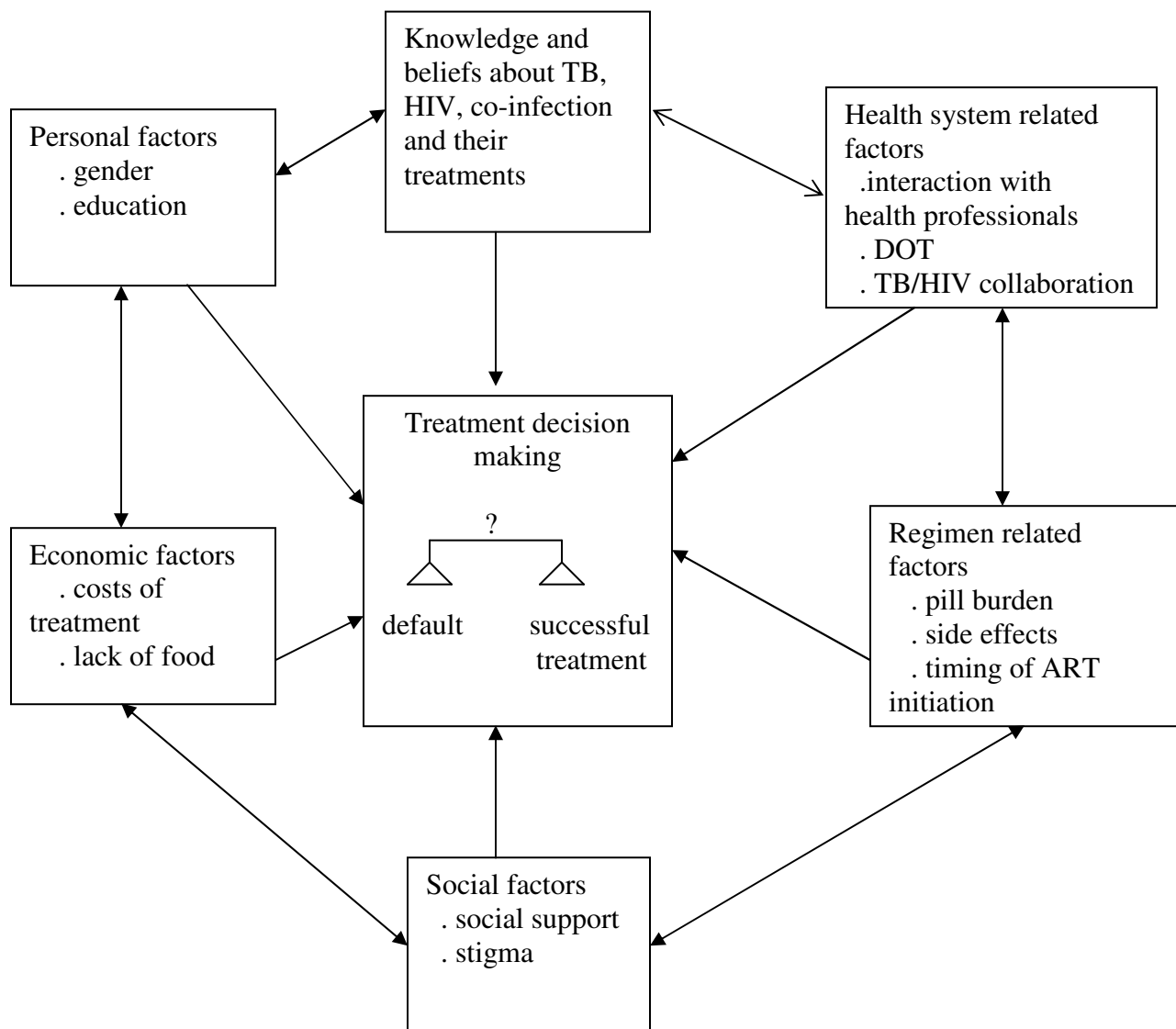


Fig. 2 Summary of factors influencing Tuberculosis treatment adherence in TB/HIV co-infected patients on concomitant treatment in Addis-Abeba, Ethiopia

## **Chapter four: Discussion and recommendations**

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We will hereunder present the discussion of important findings. We will divide the discussion into discussion of qualitative and quantitative findings to point out the important results emerging from the two components of our study and to allow for a clear flow in the discussion that would make it easier for the reader to follow; but this division does not represent a strict demarcation, since the discussions in many instances are complimentary. Fig.2 presents a summary of the findings. We will first discuss the strengths, weaknesses and limitations of our study, which are to be taken into account when looking at our results.

### **4.1. Strengths, weaknesses and limitations of the study**

#### **Weaknesses**

1. The quantitative study adopted a retrospective design, and hence, was subject to weaknesses inherent to retrospective studies namely that some important information such as for e.g. occupation, side effects was not available in the charts we reviewed
2. Since the default rate was lower than what we initially anticipated, we had a small number of cases (defaulters), hence making the power of the quantitative study weak, which has to be taken into consideration when looking at the results of the quantitative study
3. One point that can be considered as a weakness in qualitative studies is the effect of our pre-understanding, background and position which can make us ask leading questions as well as make us put emphasis on the parts that we think are important, and our study is not devoid of this weakness; but we tried to at least partially account for that through the discussion of reflexivity

#### **Strengths**

1. A major strength of our study is the fact that we used a combination of both quantitative and qualitative methods and we also combined in depth interviews and focus group discussions in our qualitative study, with triangulation that made the understanding

of adherence, which is a complex phenomenon, better. The triangulation in our study also allowed us to validate our results.

2. We had both patients' and health workers' perspectives of treatment barriers and facilitators

### **Limitations**

We conducted our study in Addis-Abeba, in three Health Centers providing both free anti-TB and ART. Our results can therefore be generalized only to patients attending treatment in similar treatment centers in Addis-Abeba. Our findings can not be generalized to other patients, for example those receiving ART treatment in hospitals or private clinics and getting TB treatment in the Health Centers, since these may have their specific barriers and facilitators, for example those related to attending two treatment centers located at different places and linked by cross-referrals. Although we only included a total of 29 patients and 9 health professionals in our qualitative study, we believe that we have, through our sampling, achieved adequate diversity among participants; in addition, the results we found were largely similar and repeatable among participants and therefore we believe that our results are transferable to similar contexts, that is Health Centers providing free anti-TB and ARV treatment in Addis-Abeba, as mentioned above.

## **4.2. Discussion of quantitative findings**

The discussion in this section is that of the HIV positive patients, who are our major group of interest, but a discussion of the differences in treatment outcomes with the HIV negative patients will be presented.

### **4.2.1. Distribution of the patients with TB/HIV co-infection**

In these patients, the proportion of females exceeded that of males (1.2/1.00). The mean age for females was 5 years lower than that of males. These findings go in parallel with the data on HIV from Ethiopia which shows that HIV prevalence among females is higher than that of males, with 55% of PLWHA being females in 2005; and which also shows that in the age group between 15-29, there are more females living with HIV/AIDS than males, whereas in the age group 30 and above, there are more males

living with HIV/AIDS than females (18). One of the reasons thought to be fuelling the HIV epidemic in Africa is actually the fact that the disease spreads in different age groups, mainly because of old males having sexual contacts with young females, vulnerable because of socio-economic and cultural reasons; as well as with females of their own age groups. Studies have found that the notification rates of TB among males are usually higher than those among females, in particular in developing countries, mainly due to socio-economic and cultural factors limiting women's access to treatment (96,97). Although we found more females than males in this study, it does not necessarily reflect an adequate access to health care by females, but might be a reflection of the fact that females are affected more than males by HIV; although it is also possible that the gender differences in accessing treatment do not exist in this set up( and that seems to be supported by the fact that we also found slightly more females than males among the HIV negative patients(F/M: 1.04/1.00)).

The mean age was 34.9 years; both HIV and TB affect largely the economically productive age groups, with 75% of cases of TB occurring in the economically productive age group (15-54 years) (13). More females were illiterate as compared to males and this follows the national and regional trends (6).

#### **4.2.2. Clinical characteristics of the TB/HIV co-infected patients**

We found that 65.3% of patients had pulmonary TB, the rest having extra pulmonary disease. Of those who had pulmonary TB, a high proportion (65.5%) were cases of smear negative TB. This is expected since HIV is known to result in higher rates of smear negative TB (8, 10). There is a high rate of smear negative TB because, due to the alteration of the normal host immune response to MTB in persons with HIV, cavitations and transfer of bacilli into respiratory secretions is markedly reduced (98). This also explains why we found a statistically significant difference in bacilloscopy status between the HIV positive and negative cohort. In addition, according to the WHO definition, a patient with TB involving extra pulmonary sites is classified as a case of pulmonary TB if there is pulmonary involvement and the smear is positive. Hence, it is very likely that a significant proportion of patients in this study classified as having pulmonary TB are cases of disseminated TB involving the lungs.

We also found that 151(60.9%) patients had CD4 count between 50 and 200 and that 44(17.7%) had a CD4 count of less than 200. Only 53(21.4%) of patients had a CD4 count greater than 200. TB accelerates the course of HIV-induced disease by activating viral replication and accentuating the decline in CD4 T cell counts (11). We also found that 44 patients were already on ART when diagnosed with TB. This shows that many patients had reached advanced stage of HIV disease without starting ART (and largely without knowing their HIV status). TB clinics had thus been the entry points for diagnosis and HIV care for many patients. Tuberculosis is an aggressive opportunistic infection that arises at higher median CD4 counts than most other opportunistic infections (23). The fact that we did not have many patients with CD4 counts of 200 and above might partially be due to the fact that health professionals delay ART in these patients until after the completion of TB treatment, based on their clinical judgment as well as patient request, since the patients included in our study were only those who had received ART during TB treatment.

It is worrisome that patients come very late for HIV treatment, after severe immune deterioration, and that necessitates raising awareness among the population about early diagnosis of HIV treatment and initiation of therapy, since ART is now freely available in governmental treatment centers.

Efavirenz containing regimens were used in the large majority (74%) of patients. The regimens available in the health centers are either efavirenz or nevirapine containing regimens. Nevirapine is not used when the patient receives rifampicin because rifampicin is an inducer of an isoenzyme which leads to increased metabolism and decreased concentration of nevirapine (39); therefore, in addition to patients already on efavirenz, patients taking ART in the intensive phase of anti-TB are started on or shifted to an efavirenz containing regimen; this explains why a large majority of patients were on an efavirenz containing regimen.

We also found that 48% of patients had another concomitant illness other than TB and HIV during TB treatment. This is expected in view of the low CD4 counts of the patients.

But it is also possible that some patients are referred to hospitals by the health centers for better evaluation and management and these cases might sometimes not be noted on the charts of the patients or the diagnosis put might not be the right ones; and patients themselves might go to hospitals or private clinics when very sick; so these factors should be put into consideration when looking at the results on concomitant illness that we recorded from the health centers, and this might also explain why we did not find any association between defaulting from treatment and concomitant illness, as we would have expected; since another illness would mean that the patient would need to take more pills, and pill burden was a major factor that patients and health professionals said would affect TB treatment adherence from our qualitative findings and it also means that the patient might have more difficulty attending treatment...

#### **4.2.3. The magnitude of default from TB treatment**

We found that there was no statistically significant difference in default rate between the co-infected patients and a comparative group of HIV negative patients treated in the same set ups, among whom default rate was 8.1%; although more patients defaulted in the HIV positive group than in the HIV negative one (26 vs. 20 defaulters). We should first point out here that there might have been a selection bias, although we tried to minimize this by including consecutive HIV negative patients going from the period of inclusion onwards. We were only able to control for the difference in age that was existent between the two groups but it is possible that other differences exist between the two groups of patients that could have affected our results, for instance differences in socio-economic status which we were not able to account for due to lack of data. Although published studies comparing socio-demographic characteristics of HIV positive and negative TB patients in Ethiopia are not to my knowledge available, an analysis of data from 34,512 VCT clients in Ethiopia showed that HIV prevalence decreased significantly with each increase in education level in both men and women (99), and another study indicated that lower income among women is also a risk factor for HIV infection (100), so such socio-demographic differences between the HIV positive and the HIV negative patients in our study might have impacted the comparison, hence, the results should be seen more as indicators of the fact that, in general, there does not seem

to be a significant difference in defaulting from TB treatment between co-infected patients on concomitant treatment and HIV negative TB patients in our set up (although default was higher in HIV positive patients), despite the former having a double burden of disease as well as being on concomitant treatment, and this needs to be confirmed with further studies. The interviews with health professionals nevertheless reinforced this finding, since all of them reported that, from their experience, there does not seem to be a major difference in adherence to TB treatment between HIV negative and positive patients, including those on concomitant treatment. As we shall discuss later, although co-infection with HIV and concomitant treatment with ART have their own negative impacts on adherence to TB treatment, such as through increased pill burden, side effects...other factors such as adverse perception of prognosis seem to positively influence adherence in co-infected patients, many of whom manage to complete treatment, although they face many difficulties. We also found out that many of the barriers and facilitators to TB treatment that patients reported are actually those that have been reported by TB patients without HIV in different contexts, as we will come to in later discussions.

Very few studies have assessed the effect of HIV on TB treatment adherence; and to my knowledge, there is no published study looking at the effect of concomitant TB/HIV treatment on TB treatment adherence. Two studies conducted in Nigeria did not find any association between HIV status and defaulting from TB treatment (45, 47). A study from Ethiopia also showed that HIV positive patients were more defaulters than HIV negative patients but that the difference was not significant (78). In these studies, patients were not on ART treatment; hence what was assessed was only the effect of the illness on adherence to TB treatment. WHO's Global Report also indicated that lower treatment success rates were found in HIV positive patients as compared to HIV negative ones, from reports gathered from over 40 countries (who were actually almost exclusively from the Americas and the European region) in 2005, mainly due to higher death rates, and, to a lesser extent, due to a higher default rate in HIV positive patients (15).

It is also important to see the default rate we found in comparison to other studies conducted in TB patients, both in Ethiopia and outside Ethiopia. The default rate of

10.5% in the co-infected patients is lower than the rates found in other studies in Ethiopia, in patients with TB only, including in Addis-Abeba where a study conducted in 1989/90 showed a default rate of 82%. The default rate we found was also lower than the rates found in the Southern region (20%) (28) and in Hadiya (18%) (32); and it was similar to the default rates found in the Northwest region where defaulters were found in 10% of the households (77) and in Oromia where a default rate of 11.3% was found. The default rate in our study was higher than that found in Jimma (6.7%) (30) and in a retrospective trend analysis in the Southern region (6%) (33). Similarly, the default rate in this study was lower than that found in Zambia (58), Nigeria (59), and Malaysia (57); higher than the default found in Uganda (56). The default rate was also lower than that found in TB patients with HIV in Nigeria (47) and Portugal (43).

Many reasons can explain the differences noted. One of the reasons is the criteria used for default; for example, although most of the studies from Ethiopia used the WHO criteria of default, in the first study from Addis-Abeba where default rate was found to be 82%, default was defined as three or more consecutive days absence in the intensive phase and/or two months absence in the continuation phase, which was a stricter definition than the WHO definition we used. WHO's definition of default actually excludes patients who might have been on treatment for less than one month and abandoned treatment, and also excludes patients who have irregular attendances in the clinics, and thus might inflate adherence. Another factor that could explain the differences, at least in terms of improvements in default rates across time and across regions within Ethiopia is, among other things, the decentralization of DOTS making the services available closer to patients which has improved through time; and which still has variable distribution across regions since the health service coverage in Ethiopia is variable, aggravated by poor transportation means (1). Two studies from Ethiopia have indicated that the introduction and expansion of DOTS resulted in significant improvements in treatment success rate as well as default rates in the Southern regions of the country (32,33). Similarly, a study from Uganda showed a high completion rate of TB treatment (92%), and that was found to be due to the way services were organized, their geographic proximity to patient's homes and the progressive use of short course



chemotherapy (56). In addition, other reasons specific to this group of TB patients, who are also HIV positive and received concomitant ARV treatment, might explain the differences noted, as well as socio-economic and cultural factors specific to different set ups. But the results in general indicate that the default rate to TB treatment that we found in this group is among the lowest found in studies from Ethiopia so far.

#### **4.2.4. Timing of default**

Most of the defaults in this study occurred in the continuation phase of treatment, and consistent evidence exists in the literature that most defaults from anti-TB occur in the continuation phase of treatment, with studies both from Ethiopia and outside Ethiopia showing that majority of patients default in the continuation phase of treatment (28, 29, 59, 69, 75). The most common reason given in the literature is a feeling of improvement that patients may get after having been on treatment for a while that would encourage them to stop treatment, mainly in areas where improvement is equated to cure. A qualitative study from Addis-Ababa where the effect of time was assessed indicated that patients usually lost support from families and community as treatment progresses, and hence are forced to discontinue treatment in the later stages of treatment (31). Our qualitative data also suggests that patients usually struggle to continue treatment as much as their resources allow; despite medical and socio-economic problems that they face, and the decision to stop treatment usually happens after the patient feels that all means have been exhausted, or when they feel that the pressure they are exerting on their families is too much. Thus, although it is the intensive phase with daily clinic attendance, severe clinical symptoms and severe side effects (mainly in those started early on ART) that patients describe as being the most challenging, patients usually manage to go through it and exhaust all their means while doing so; forcing them to quit treatment in the continuation phase. For those patients whose jobs are compromised because of the requirements of treatment, subjective improvement might also lead to the patients wanting to return to their daily works. Many patients interviewed pointed to the fact that improvement in weight and strength is very important to avoid stigma related to HIV; hence, once the patients regain weight and strength after being on TB treatment for a while, they might stop treatment over more pressing issues. It is important to mention

here that WHO's definition excludes patients who leave treatment within the first month of treatment, and that patients might actually leave treatment in that period because of factors such as immune reconstitution etc.

Nevertheless, the continuation phase is a critical phase for adherence. Health professionals should be aware of this fact, and adherence counseling which is usually given only in the beginning of treatment should be repeated at later stages, when patients come for drug refills.

#### **4.2.5. The impact of timing of ART initiation on TB treatment adherence**

We found in our quantitative study a significant association between timing of ART treatment and defaulting from TB treatment. Patients initiated on ART in the intensive phase of anti-TB treatment were found to have a 9 times higher chance of defaulting than those started in the continuation phase. These results confirm the concerns on the side of many about the possibility of adherence being potentially affected if ART is started early in the treatment of TB (23, 39, 101), a concern that has also been taken into consideration when setting guidelines regarding timing of ART initiation in the course of TB treatment. Many reasons could explain this finding. First, patients are usually diagnosed with HIV when coming for TB treatment and the initial phase is usually difficult in terms of coping with the diagnosis of two illnesses, as was also revealed by the patients we interviewed. Many patients described a loss of hope in the initial phase, which they usually overcame, but after some time. Therefore, patients' readiness for treatment might be compromised initially. On top of that, drug intolerance might be worse for these patients since multiple treatments are initiated at close times. Some patients interviewed had a belief that their body would adapt to the TB drugs after some time and get ready for the ART if they are provided ART at a later time. Patients started on ART drugs early in their TB treatment can also be predisposed to immune reconstitution inflammatory syndrome, presenting as transient worsening or appearance of new signs and symptoms of TB (23) and due to the restoration of pathogen specific immune reactivity against pre-existing pathogens leading to inflammatory reactions in infected tissues (39); and that can also potentially affect adherence in these patients. A

study from Malawi had indicated that adherence to ART was better in those initiated on ART in the continuation phase of TB treatment as compared to those immediately started on it, due to better readiness (46). Although health professionals said that patients' readiness was assessed before the initiation of ARV, some patients interviewed said that they started treatment because health professionals told them that they need it. Hence, despite fear of concomitant treatment and stress related to the diagnosis of two chronic illnesses, patients might agree to initiate ART without being ready for it and subsequently default from either or both treatments.

There is strong evidence that ART improves mortality of patients with TB, which is highest in the first two months of treatment; mainly when introduced early (11, 23, 39, 44, 45). Therefore, delaying ART might not be a good option for this group of patients, weighing against the possibility of mortality, although adherence might be compromised. Rather, such patients for whom ART is introduced early in the course of TB treatment need further adherence counseling and assistance from health professionals; and should be followed thoroughly for occurrence of side effects or immune reconstitution syndrome and managed accordingly. Patients need to have a say in their treatment and should be thoroughly counseled and informed about risks and benefits of starting ART early, and should be allowed to make decisions themselves.

Patients started on ART before the initiation of anti-TB also had a higher default than those started in the continuation phase. That might be due to the fact that patients give up hope on treatment when developing TB after taking ART for some time. The overall period of concomitant treatment is also longer for these patients meaning that they have a longer period of exposure to problems associated to concomitant treatment.

#### **4.2.6. The impact of gender on TB treatment adherence**

We found in the quantitative study that male sex is associated with defaulting from treatment; although the difference was not statistically significant in the HIV negative patients, which might be due to a lack of power in the study. Studies from Ethiopia (32), Pakistan (102), Thailand (50), Madagascar (55), Nigeria (59), India (103), have also indicated that male sex is associated with defaulting from TB treatment, whereas other

studies from Ethiopia (28), Portugal (43), Zambia (58), did not find any relationship between sex and defaulting.

The reason why more males than females default from treatment in our set up might be related to the fact that more men than women are employed, therefore find it difficult to adjust their working schedules with attendances at the clinic. In our interviews, we also found that a major concern of males was the impact of treatment on their jobs and consequently on their income and that of their family as a whole because they were providing for their families as well. Similar reasons were given for why more males default in Madagascar (55) and Nigeria (59). Some health professionals interviewed said that females are more responsible than males and that their experience is that females adhere better to treatment than males. Females are indeed responsible, and raised worry about what would happen to their siblings if they did not recover from their illness, and hence seemed motivated to take their treatment and get cured. But what might appear as irresponsible on males' side by discontinuing treatment might actually reflect a responsibility they assume by continuing their works and providing incomes for themselves and families at the expense of their treatment.

As discussed earlier, females might have more problems in accessing health care and in being notified to treatment facilities because of socio-economic factors and gender inequalities; so there is an argument that barriers to diagnosis of TB in women screen out those women most likely to default and that those who overcome diagnostic barriers are likely to be highly motivated, hence most likely to adhere to treatment (97), and this possibility can not be ruled out in our set up as well.

What might help in this case is addressing the factors that make males particularly vulnerable to defaulting. The daily routines of DOT and additional attendances at the ART clinics do not fit working schedules for many as we will discuss later and addressing that issue might solve the problem. Health professionals should be aware of this potential gender difference in default and its potential causes and they should assist patients accordingly.

#### **4.2.7. The impact of education on TB treatment adherence**

We found a significant association between defaulting from treatment and education, with patients with primary and below education having a higher chance of defaulting than patients with secondary and above education. It is first important to explain that in our record review, we were not able to retrieve data on income or occupation of the patients, since, although occupation should have been filled out in the ART charts, it was not the case in many instances, and hence, we had to take it out from our analysis. Hence, it is possible that in our study, level of education was confounded by the economic status of the patient, since it is likely that patients with higher education would have a better chance of getting a job and having a better income than those with no education, although it is difficult to know to what extent the confounding was. And income/economic status of the patient could potentially affect adherence as will be discussed in later sections.

Nevertheless, education can impact on adherence to treatment because it might be related with knowledge about the disease, the drugs, their side effects, and the necessity for adherence and for taking treatment for eight months. Adequate knowledge about the illness and its treatment have been shown to be associated with better adherence in many studies, both from Ethiopia and outside Ethiopia (40, 52, 53, 54, 75, 82). From our interviews, it also appears like patients who ask for information from health professionals about their illness and the treatment were those who were more educated; and therefore these might get the necessary information from health professionals, which might also explain why more educated patients adhere to treatment better. A similar tendency was noted by Sagbakken in her study conducted among TB patients in Addis-Abeba in 2001/2, with less educated patients being more hesitant to approach health professionals as well as being the ones receiving less information from health professionals (104). Studies from Ethiopia (28, 29), Malaysia (57), and Zambia (58) did not show an association between education and defaulting. One of the reasons might be the fact that there is better awareness about TB and its treatment in the community secondary to health education/communication about TB provided for the community at large in some set ups. These studies are also conducted in patients with TB only, and our patients were co-infected patients taking complex treatment and might face more complex issues such as

understanding the effect of pill burden, concomitant illness, side effects...As we will discuss in the following section, many misperceptions exist with regard to the illnesses and their treatment, and that can have an impact on adherence to TB treatment.

### **4.3. Discussion of qualitative findings**

#### **4.3.1. Understanding about TB, HIV, co-infection and the impact on TB treatment**

We found that there were misperceptions about the origins of TB, which included its association with *bird*, as well as other factors such as excessive sun, mud, smoking, alcohol, sexual contact. Patients also believed that lack of food would predispose to TB. Misperceptions about TB have been found in other studies from Ethiopia where, in addition to the factors mentioned above, other factors such as evil spirit and consumption of contaminated food and water were incriminated in the causation of TB (76, 77, 81). Similarly, a study from South Africa showed that mine work, malnutrition, infected food, disobeying traditional rules were thought of as causes for TB, in addition to smoking, alcohol, and sex (67). In Kenya, a study found that the origins of TB were thought to be: alcohol, smoking, exposure to cold, hard work, hereditary (68). The importance of *bird* as a causative agent for TB is particularly significant, and it seems like that belief has at times been supported or reinforced by health professionals, because some felt like it is too difficult for patients to understand the medical explanations for TB, or there was no sufficient time to discuss with patients. The belief in *bird* as a causative agent for TB adversely affected treatment because patients first tried home remedies such as warm drinks and avoidance of further exposure to cold and therefore were delayed in seeking medical advice. This is particularly dangerous in this group of patients co-infected with HIV since it also means that the untreated TB infection causes further deterioration in the immune status of the patient; which can also potentially affect adherence because patients come at a late stage for treatment when their symptoms have progressed, which makes clinic attendances difficult, tolerability of drugs worse, worsen the economic situation of both the patient and/or families because of inability to work, ... . In addition, it resulted in some patients ascribing their HIV diagnosis to their delay in seeking treatment. A previous study from Ethiopia had indicated that self treatment was associated with treatment delay in the Amhara region (27); another study in the Southern region also

showed that 70% of patients initially thought that the symptoms would disappear without clinical treatment (26). The reason for delayed treatment in these studies might be due to similar beliefs about TB in those areas as well. Sagbakken similarly indicates that the belief in *bird* as a causative agent of TB guides different beliefs and activities in TB patients, starting from the time of symptom recognition, to when treatment is initiated; subsequently leading to delay in diagnosis, and indirectly affecting treatment adherence (104).

In this study, the absolute majority of patients interviewed knew that there is a relationship between TB and HIV. Even in 1997 when the epidemic did not reach its current dimension, a study from the rural area had indicated that 20% of patients knew there is an association between TB and HIV (77). But misperceptions as to the relationship between the two illnesses existed. The most common one being that TB turned into HIV. A previous study from Addis-Ababa had indicated that such a belief exists among patients, with AIDS perceived as a second stage of TB (81). Few understood the relationship between the two illnesses as being due to the effect of HIV on their body. For some patients, the knowledge about the association between TB and HIV came from what they heard in the community and others claimed they heard that on the media. It is thus evident, as also explained by health professionals, that information disseminated by the media was misunderstood by patients.

Patients also explained that not all patients with TB have HIV, although they believed the most common type of TB was the HIV associated one, and said that a patient with TB only and a patient with TB and HIV can be differentiated based on their weight and strength, in addition to darkening of the skin, which is due to HIV. It was found in a study from Thailand that half of the patients interviewed believed that AIDS patients were different from TB patients because AIDS patients were too weak to walk while TB patients could walk, hence reflecting the picture of an HIV patient that they had (72). Most patients believed that this belief is shared by the community and hence feared stigma, especially when they lost weight, became weak and developed skin changes. This in turn affected their treatment (the effect of stigma on adherence to treatment will be

discussed later). These beliefs might be due to the fact that ART was only introduced in recent years in Ethiopia, and many in the community have seen terminally ill patients in the pre-ART era, many of whom they lost, and the popular image of a patient with HIV infection is a patient who has lost weight, has skin lesions, and coughs. And this image has probably been supported by the media's portrayal of HIV patients. Being from Addis-Abeba myself, I have also experienced seeing many people being suspected of having HIV if they have been ill for a while, have lost weight, and appear weak.

We also found that the difference in knowledge between TB and HIV is significant, many knowing the major routes of transmission of HIV. This might be a reflection of the media's coverage of the illness, and many indeed explained that they heard about HIV in the media. HIV has also been well covered in different health education campaigns that have involved schools, communities, work places .... But TB seems to have been neglected by the media and by health education campaigns, and if education was given about TB, it has most often been in relation to HIV. A study from Thailand also found that the community had a higher awareness about HIV as compared to TB, and that an increase in awareness about AIDS had not been accompanied by a rise in understanding of TB control (72). The HIV epidemic has been followed by unprecedented funding from international donors, which has made it possible to make media advertisements, dramas, health education campaigns, with involvement of multiple NGOs. But TB has not gotten the same attention or the same amount of donor involvement that HIV has had, despite the heavy burden of disease that TB imposes in many areas of the world. Whether TB will receive better attention now because of the tight association with HIV which is becoming apparent in many countries and whether better collaboration between TB and HIV programs will include raising awareness about TB as well remains to be seen. One of the aspects of collaboration should be raising awareness about the relationship between the two diseases.

One finding that was interesting was that many patients believed in the curability of TB, as well as in the efficacy of TB treatment, although some thought it might be more difficult and might take more time for them, because they also had HIV infection. Even



those who believed that TB had changed into HIV still thought that they could take drugs and get cured from the TB, but that the HIV would persist. This, as also mentioned by some health professionals, might be a result of the fact that patients have seen people with TB in their community cured after receiving treatment (also shown in a study from Pakistan(65)), and were also encouraged by the changes that they see in patients at the clinic. Studies have shown that belief in the efficacy of treatment facilitates adherence to TB treatment (52, 53, 54); while other studies have shown that patients' adherence was adversely affected because of the belief that TB is incurable or the treatment inefficient, or that alternative treatment such as traditional medicine is better (51, 52, 53, 67, 68). Although some authors had raised concern about the possibility of the relation between TB and HIV enhancing the questioning of the curability of TB (68), there was no strong evidence of it in this study.

But, for many patients, prognosis of TB treatment in the presence of HIV infection was believed to be poorer as compared to HIV negative patients, and that had at times been reinforced by warnings from health professionals about the danger of TB linked with HIV. That seemed to positively influence adherence because patients believed in the importance of taking treatment in order to survive, and many health professionals also said that it encouraged patients to take treatment. That might mean more motivation for this group of patients as compared to HIV negative patients, some of whom might discontinue treatment, mainly when they feel better. In addition, health professionals also argued that these patients had severe symptoms and were eager to take drugs to improve and not to get these symptoms again. Other studies have also suggested that patients experiencing more severe symptoms were more likely to adhere, possibly because of a fear of becoming more ill (52). These beliefs actually correlate to the threat of illness and the consequences of diseases which are believed to influence adherence behavior (92).

Use of traditional medicine for TB treatment was not reported by participants in our study. Traditional medicine was commonly used in the past in Ethiopia, with as high as 80% of people estimated to be relying on it in 1991 (3), mainly due to lack of access to

modern treatment but also due to persisting beliefs in its efficacy, mainly in rural areas. But participants in our study said that traditional medicine is not a good option for TB, reinforcing their belief in the efficacy of anti-TB treatment. In addition, some seem to have lost confidence in traditional medicine in general. The fact that the health service coverage is high, that patients see people in their communities getting treated and cured from TB by using modern anti-TB drugs can also explain why traditional medicine is not used for TB.

The issue of use of *tsebel* or holy water had raised concerns in recent years because of many abandoning ART treatment over it; but we found in our study that patients now are taking *tsebel* together with both anti-TB and ART, and this follows the preaching of concomitant use by priests in the orthodox church, as explained by health professionals, after the orthodox church was approached by health professionals. This is a reflection that the health system and religious leaders can work together to make changes, since religious leaders are quite influential in the community.

So what we found in summary is that misperceptions exist with regard to TB and TB/HIV co-infection. Many patients relied on information that they got from the community, as well as the media; hence what was evident was the role that the popular sector was playing in terms of defining the illnesses, their causations, whether treatment will be beneficial, as well as when to consult the professional sector. The patients we interviewed have passed through the professional sector, many having been there for many months, but still many of their beliefs were those defined within the popular sector, a reflection that the professional sector has not been a major source of information for the patients; at times, the beliefs in the popular sector have even been reinforced by the professional sector such as for instance the effect of bird as a causative agent for TB, further reinforcing the misperceptions. The folk sector seems to have gradually lost importance in the setting, at least in relation to TB treatment, although the sacred part retains its importance, as exemplified by the high use of holy water together with TB treatment in patients. The use of holy water together with modern treatments is a result of the cooperation between the professional and the folk sectors, which yielded fruitful

results by encouraging concomitant intake of holy water and drugs instead of abandoning treatment over *tsebel*, which had been the case in the past.

What we largely discussed is what Cummings et al abstracted in two of their categories as factors affecting treatment adherence, that is items dealing with the individual's attitude toward health care, such as beliefs in the benefit of treatment and beliefs about the quality of medical care provided, and items concerning the threat of illness, such as the individual's perception of symptoms and beliefs about susceptibility to, and consequences of, disease (92). We found that these factors largely influenced patients' treatment adherence; mainly that the beliefs in the benefits of treatment and the belief in the severity of TB treatment when related to HIV infection and its potential consequence, that is death, positively influenced adherence in these patients despite many difficulties that they reported.

Our recommendation with this regard is that much needs to be done to raise awareness about TB/HIV for patients and for the community at large. The MOH calls for Advocacy, Communication and Social Mobilization (ACSM), as one of the components of TB/HIV collaborative activities, with the aim of raising awareness about TB/HIV among the community in general and those at risk of TB/HIV in particular and to mobilize them ultimately to, among other things, enhance comprehensive patient care (18). This is indeed very important and collaborative communication and social mobilization strategies need to be set, that ensure that coherent messages about TB, HIV, and TB/HIV are passed along. Health education and communication should be delivered in health facilities, households, schools, traditional social meetings and in religious institutions whenever possible. The messages should be made culturally sensitive, and adjusted to the audience that is to be addressed. Religious leaders and community leaders are influential and their participation is very critical in order to reach the community at large. Experience from the southern region has shown that organization of patients into DOTS clubs, together with involvement of other influential community members such as priests and Muslim religious leaders and community elders has yielded remarkable results in improving knowledge about TB as well as improving adherence to treatment and

increasing awareness about TB and its treatment (79,80). Lessons should be derived from this and adopted to the context in Addis-Abeba.

The media is also a channel that reaches many people at once and should be used to give health education, and it seems that patients listen frequently to messages on the media, with many referring to knowledge gained from the media in our study but the messages conveyed should be made simple and sensitive to avoid misunderstandings as well as further stigmatization as will be discussed later.

### **4.3.2. Regimen related factors and their impact on adherence**

#### **4.3.2.1. Pill burden**

Pill burden was one of the most important problems that both patients and health professionals interviewed said affected treatment in co-infected patients on concomitant treatment. Patients not only ascribed some of their symptoms to pill burden but also feared that their “weakened” body might not be able to tolerate so many pills. In this study, pill burden was seen as a major problem by patients because patients believed that the number of pills swallowed determined the degree of “harm” that the drugs could potentially cause to the body but also because they believed that the amount and quality of food needed is proportional to the number of drugs swallowed. Studies have previously indicated that pill burden adversely affects adherence to treatment (36, 40, 73, 105). In addition, some found the dosing schedule difficult since they had to swallow anti-TB, ART and cotrimoxazole, with ARV drugs twice a day; which resulted in forgetfulness as well as difficulty to adjust drugs with working routines. The effect of dosing frequency has also been discussed in the literature and frequent dosing has been found to be associated with poorer adherence to treatment, whereas decreased frequency was associated with better adherence (40, 41, 42, 73).

Recently, fixed dose combination ARV drugs have been introduced and this will assist patients in terms of alleviating the problem of pill burden. Introduction of once daily doses of ART in the future would further assist patients. In addition, health workers

should thoroughly discuss and plan together with individual patients the schedule that fits the most with their daily routines instead of setting similar schedules for all patients. The fear of patients about the effect of many pills on the body should also be addressed through health communication as well as the issue of necessity of food proportional to pills swallowed, as we will discuss later.

#### **4.3.2.2. The impact of side effects**

Multiple side effects were reported by patients and this is expected because both anti-TB and ARV drugs are known to have side effects, some of which are overlapping. In addition, patients feared side effects that they heard about in the community. Beliefs such as the weak body of an HIV positive patient not tolerating drugs were described. Health professionals were also aware of these beliefs among patients. Worsening of symptoms after start of treatment was also reported, and patients ascribed that to the drugs. Most patients interviewed also said that they were not informed about side effects, and were unable to know whether it was the TB drugs or the ART drugs that gave them the side effects, and had to rely on their own beliefs about side effects. One patient discontinued all treatments, not able to know which drug gave him the side effect, while another believed it was due to TB drugs and discontinued those. Side effects, both experienced and perceived, have been known to affect adherence in many studies on adherence to anti-TB, in both HIV positive and HIV negative patients (29, 43, 50, 52, 54, 58, 74) and side effects were also found to affect adherence to ART (73, 82), often because patients were not warned about those.

Some of these side effects might be transient or otherwise could be managed but some patients were unaware of it and believed discontinuing treatment is the solution, and did not seek treatment for it. Health professionals should inform patients about potential side effects. Early detection and management of side effects would also help patients. Health communication should include educating patients and the community about anti-TB and ART drugs and dealing with beliefs that exist about side effects, since what patients relate to is largely the perceived side effects of anti-TB and HIV drugs in the popular sector, although many have actually experienced side effects while on treatment.

It is worth noting here that the impact of side effects and pill burden are affected by popular beliefs about drugs and side effects and how patients and the community perceive those; these therefore also become part of factors related to patients' beliefs, as well as actual experienced regimen related factors associated with patient treatment. Therefore the same solution to address popular misperceptions should also address side effects and pill burden, giving patients and the community a better understanding of these.

### **4.3.3. Health service related factors and their impact on adherence**

#### **4.3.3.1. The impact of DOT**

DOT was difficult for many because of the economic constraints related to transportation costs as well as its clash with job routines, threatening the jobs of some; and patients in addition were also attending HIV clinics. In addition, it was physically demanding for those who were very sick, and those had to be accompanied by their families, every day for the first two months. In those cases, the income of family members was also compromised, with patients feeling guilty for imposing a burden on their family. A previous study from Addis-Abeba also showed that DOT was physically demanding for patients, mainly for those who were ill, and showed that it incurred transportation and opportunity costs for patients, many of whom were unable to hold on to their jobs (31). For a few, it was also the lack of autonomy that they were finding difficult to accept and that was also reflected by health professionals' comments as well. Therefore patients might usually face the dilemma of choosing between their incomes versus daily attendances at the clinic and discontinue treatment if the loss of income is beyond what they can tolerate. In addition, it might be difficult for a patient to comply with a routine he/she doesn't believe in. Other studies have also indicated that patients face difficulties with the daily routines of DOT (31, 52, 53, 64).

Although health professionals raised concern about the improper intake of drugs without DOT, many also agree that the routine is difficult for patients. There was also variable degree of flexibility among them, some being strict in terms of following guidelines, others being more flexible. The guideline indeed says that patients should be supervised while swallowing pills the first two months but some personal judgment might

be necessary, mainly when very ill patients are involved, or if patients have very pressing issues that make it difficult for them to attend treatment. TB treatment approach was set up mainly from a public health perspective, according to which infectious cases should be treated to cut the chain of transmission to others and treatment supervised in order to protect rifampicin from the occurrence of drug resistance. What is taken into account less is how this affects individual patients, both socio-economically, but also in terms of autonomy.

The possibility of community based DOT, in conjunction with local NGOs already working with HIV patients should be considered, after proper training of community workers, although there might be limitations due to HIV related stigma. The ministry of health also reported the following barriers to the implementation of community TB and TB/HIV care: poverty and basic needs requirement that hinder community members from participation in the care of their own sick, a difficulty to maintain motivation and awareness, and financial constraints faced by community organization (15). Use of already established NGOs working with patients at community level might help alleviate some of these problems. This might not only provide support with treatment but also emotional and social support for patients since some, as found in our qualitative study, were not telling about their illnesses to their families or neighbors and lacked the necessary social support. A review of trials conducted in low, middle and high income countries showed no evidence of superiority of DOT versus self supervision in terms of cure and treatment completion. Supervision by health professionals, lay health worker, and family/community member was similar in terms of treatment completion (71). In set ups like ours where economic constraints and unstable daily jobs are common, DOT at health facilities might not be the right option for management for all. Encouraging results have already been obtained in a community based DOTS programme in the Oromia region of the country (13).

It is also important to change the daily routines of DOT into encounters with patients from which they benefit more in terms of getting information and support from health professionals, and that might be more motivating for patients. Flexibility at least in terms

of appointment hours for patients would assist some patients like students who can come and collect their drugs as per their class schedules. The necessity for daily supervision of treatment should be clearly explained to patients, who should know that supervision when it comes to TB treatment is a universal phenomenon, and not something imposed in that particular set up.

Another concern for many patients was that receiving treatment in nearby health centers would predispose them to stigma. Although some patients prefer being treated in distant health centers, health professionals could not accept those because the guideline is that patients should be treated within their catchments area. The regulations have recently changed for HIV patients who can now be treated in the health center of their choice, and the same solution might be necessary for TB treatment as well, although this might result in unequal distribution of patients within health centers with overburdening of some of them.

#### **4.3.3.2. TB/HIV collaboration**

The HIV epidemic has challenged DOTS as a sole tuberculosis control strategy for Africa, since even strong programs can not adequately compensate for the rising susceptibility to tuberculosis at the population level that occurs as HIV prevalence increases (23). The need for TB/HIV collaboration is therefore important in many aspects.

One barrier to collaboration has been the difference in how HIV/AIDS and tuberculosis surveillance, diagnosis and treatment have traditionally been approached. TB control programs have adopted a public-health approach, with major aims of controlling TB transmission and avoidance of drug resistance whereas HIV/AIDS programs have adopted a patient centered approach (23). In addition, separate administration and funding have also played their role (106).

Most health professionals (one being the exception) we interviewed said that the collaboration is very weak. There was a fear that different information might be given or patients lost in between. Although TB clinics were serving as points of entry into HIV clinics for many patients, after referral to the HIV clinics, those were treated as any TB



patient, and no link exists between the two clinics concerning the management of individual patients, and HIV clinics were leaving the whole responsibility of TB treatment to the TB clinics, hence, the traditional way of working is persisting in the clinics. Joint trainings or meetings were not organized. Unless health professionals are trained in the management of both illnesses and have a common recording system for common patients and regular occasions to meet and discuss their patients and their collaborative activity, the traditional way of working will persist, and health professionals will only feel responsible for the management of either illness.

Patients also felt that the two clinics were not working together in terms of arranging their schedules and managing their treatment. This can adversely affect patients' treatment because they get treated by different health professionals who manage their illnesses separately, and patients might be discouraged by repeated queuing at the health centers on different days which might compromise their jobs, increase transportation costs, and some patients pointed this fact in the interviews.

Provision of training in both HIV and TB management for health professionals in both clinics and establishment of a system of recording whereby common patients are easily identified should be set. That would facilitate the management of side effects as well, and would allow health professionals to notify each other when a patient initiates or terminates or changes treatment or when he disappears from either clinic. The new registers in the TB clinics that were recently introduced are important. Arranging convenient schedules at the two clinics so that patients are spared from repeated visits at the health center would also assist patients. Successful integration of TB/HIV treatment has resulted in excellent adherence and TB and HIV outcomes in a rural setting in South Africa (104), and three case studies from Malawi and South Africa of TB/HIV collaboration and integration also gave successful results (107).

#### **4.3.3.3. The role of the health personnel**

This has to some extent been discussed earlier in relation to the routines of DOT and information provided. What we found in this study in general is that patients felt satisfied by the health personnel in both TB and HIV clinics and appreciated the degree of

compassion from their side. Many were satisfied with the counseling they initially received upon diagnosis of HIV or concomitant illnesses. That encouraged many patients to regain hope and continue treatment, some saying that they would not have been able to take their treatments and finish it without the support from health professionals.

However, what was notable as well is that, after 8 months of treatment, most patients knew little about their illnesses (in particular TB and co-infection), the medications, their side effects..., reasons which have led to discontinuation of treatment for e.g. through lack of knowledge about side effects, screening of which drug should be discontinued... Most health professionals are aware of the lack of health education / communication provided to the patients, and said that lack of time was a major barrier. The problem was aggravated by the fact that patients themselves do not ask questions to health professionals, and some replied that it is because they believe health professionals do not have time to reply to their questions. What was apparent was that many of these patients accepted the fact that they did not receive information as something “normal”, most probably because of the cultural gap that exists between patients and health professionals; with a hierarchy that places health professionals far above and makes it difficult for patients to ask questions. This can also partly be due to the fact that many have been through similar encounters with health professionals previously, and had similar expectations when coming to the clinics. Few health professionals also felt that some detailed explanations might confuse patients more. What was apparent was also the fact that more educated patients felt more comfortable asking questions and discussing their illnesses with health professionals. This is probably because one potential barrier between the patient and the health professional is broken, that is the level of education, making patients less scared to ask questions. Health professionals might also feel that providing further information for such patients would not lead to “confusion”, because they are educated.

Whatever the reason is, the information gap was therefore wide. Some information regarding what to consume and what to avoid, and not to stop treatment was told to most patients, in what seems like a routine kind of information provision, in which patients

passively received information, at times not even understanding the logic behind it, or misunderstanding the information. Sagbakken also noted in her study in Addis-Abeba that there was a lack of dialogue between patients and health professionals, with consequent lack of information and knowledge provided to patients (104).

Previous studies have shown that patient-provider communication affects adherence. Good relationships such as those in which trust was established, a supportive clinic environment, adequate time spent explaining the disease facilitating adherence in the consecutive studies (40, 51, 63), whereas poor patient provider relationships, including those with lack of information from health professionals adversely affected adherence (53, 64). In addition, the fact that there is little flexibility in DOT routines on the side of some health professionals who at times refuse to give drugs to relatives of very sick patients, affects the patient-provider relationship and threatens adherence, and a previous study from Addis-Abeba described similar results (31).

It is encouraging that health professionals are showing compassion to patients and assisting them with their treatment. Although there is usually a lack of time in the clinics because of a high number of patients coming to the clinics, health professionals should make it a routine to give at least the most important information to patients, in a simple and understandable manner. In addition, patient education materials such as the pamphlets available in the HIV clinics should also be prepared for TB patients. Patients should be empowered and encouraged to have discussions with health professionals, and have a say in their treatments as well. This will need a commitment from the side of health professionals as well, who are the “sources” of the information, because one important aspect of health communication is the fact that among other things, the receiver should feel close to the source, believe in its trustworthiness (108). Similarly, communication is more accepted when the person perceives the source to be similar to him/her (108). Hence, use of ex-TB patients to give health education to patients might be a good option because patients might relate to them more, in addition to information provided by health professionals; this is actually being practiced in the HIV clinics with relation to HIV where expert patients (trained HIV positive patients) give health

education to patients. Persisting beliefs about TB among some health professionals such as the effect of bird and sexuality on TB treatment should also be addressed, since it affects both patients' belief and it also leads them to bring such information back to the community as information supported by health professionals. Patients will actually serve as sources of information to their families and to the community at large, since they might be considered as having good knowledge about the disease because they have experienced it and attended treatment facilities, and patients developing illness in particular might consult these patients subsequently, hence educating patients means allowing them to disseminate adequate information further.

What is interesting is that health professionals seem to be largely aware of the factors that influence treatment in their patients, as we found that their perceived barriers and facilitators of treatment are very similar to those reported by patients, including the impact of health service related factors, such as the information provided to patients. Hence, that should create a solid ground for interventions involving health personnel. Adherence counseling is very much emphasized upon in the treatment of HIV where it is provided to all patients prior to initiation of treatment. Adherence counseling is also needed for TB treatment, and potential factors affecting treatment should be addressed, with family involvement whenever possible. Since adherence is a dynamic process, adherence counseling should be done throughout the course of the eight month treatment, as much as possible.

#### **4.3.4. The social influence**

The importance of society surrounding the individual on adherence to treatment has been indicated in the abstraction from Cummings et al, where it was categorized as “items dealing with the individual's social interactions and with social norms and social structure”, and this is what we will discuss next through the discussion of stigma and social support.

#### 4.3.4.1. Stigma

Several definitions have been given to stigma along the years. One definition is: “a social process or related personal experience characterized by exclusion, rejection, blame or devaluation that result from experience or reasonable anticipation of an adverse social judgment about a person or group. In health related stigma, this judgment is based on an enduring feature of identity conferred by a health problem or health related condition” (Weiss and Ramakrishna, 2001) (109).

What we found in this study is that patients believed that both TB and HIV could lead to stigma; but feared more HIV related stigma. In many instances, when asked about TB related stigma, patients actually emphasized that it was HIV related stigma that was predominant. There was a high degree of felt stigma, which is different from enacted stigma. Felt stigma refers to the fear of being discriminated against, whereas enacted stigma refers to the actual experience of a prejudicial act (110). That was because many had seen patients with HIV suffer from stigma and discrimination in their communities, and feared the same will happen to them, and felt that TB will predispose them to HIV related stigma because of the association between the two diseases; that was particularly worrisome for those who had lost weight and experienced generalized weakness, because they believed that it would make people label them as having HIV as well. There were nevertheless experiences of enacted stigma due to TB among patients. Social isolation and interruption of visits by neighbors and relatives were reported by patients.

A mechanism that was adopted to fight against stigma among patients in our study was “covering”, which is a strategy whereby a person with multiple discreditable attributes covers a dominant stigma with one that is less dominant (Goffman, 1963) (110). Hence, some patients disclosed TB infection over HIV. HIV is associated with behavior that is thought of as inappropriate (many are aware that HIV is sexually transmitted, and it is therefore at large believed to be related to behavior such as promiscuity) whereas TB is usually believed to be due to factors such as *bird*, hence it is expected that more stigma will be attached to HIV than TB alone. Sagbakken, in her study in Addis-Abeba, explained that people are exposed to different types of stigma related to TB, depending

on how the neighborhood behaves in relation to their illness, which follows a cognitive continuum which; on the one hand, contains a curable type of TB associated with bird, and on the other has the non curable type of TB or AIDS, associated with sinful behavior (102). A study from South Africa also found that co-infected patients hid their HIV status and only told about their TB diagnosis due to fear of stigma (110). A study from Thailand also showed that although both TB and HIV are stigmatized, more stigma was attached to HIV, and that patients got delayed in seeking treatment or defaulted from treatment of TB when they suspected they have HIV and feared for it to be detected (72). But other patients in the study did not tell about TB as well; even to close families, because they knew that there was a belief that one has most probably HIV if he has TB. For other patients, stigma was due to the fact that they were infectious, and reported incidences such as families separating their eating utensils.

Felt stigma and /or enacted stigma had negative impacts on the treatment of patients. Patients usually lost a support system, the social support, by not telling about their illness. These patients would have benefited from financial and moral support from families, relatives. It also made it difficult for patients to be treated in the health centers located in their neighborhoods, for fear of being seen by community members. That created additional stress for patients, some of whom were constantly hiding their medication intake, both anti-TB and ARV. TB related stigma was found to affect patient treatment and in particular adherence to treatment in many studies. TB related stigma was reported in a study from Ethiopia published in 1996, which showed that patients and family members were excluded from social and religious ceremonies for fear of contagion (76). Another study also showed that the majority of respondents were not attending social gathering and festivities with TB patients on treatment (77). Although contagion as a source of stigma was not stressed upon by patients in our study, it is most probably because it was overshadowed by a biggest fear of stigma associated with HIV. Other studies have similarly indicated that TB related stigma due to contagion, as well as attribution of the illness to breakage of cultural rules... had adversely affected patient treatment (52, 53, 63, 65, 67, 68). A study from Pakistan (65) indicated that the stigma might be worse for females who risked divorce and low chance of marriage. Low rates of

HIV testing acceptability in some regions of Ethiopia might also reflect a fear of stigma associated with the diagnosis of HIV (84). A study conducted in Nigeria indicated that one of the reasons from TB treatment default in HIV patients was the fact that stigma and discrimination forced some HIV positive patients to relocate (47). The impact of HIV related stigma on ART has also been reported from a study in Uganda, Tanzania and Botswana with patients having to hide their medication intake for fear of being stigmatized, which resulted irregular drug intakes and loss of social support (74).

An important intervention would therefore be combating TB and HIV related stigma, and both patients and health professionals noted an improvement in HIV related stigma along the years, which is encouraging. This can be done through raising awareness about TB, HIV and co-infection. In addition, the community should be informed that HIV has now become a chronic manageable disease with the introduction of HAART, since some of the stigma related to HIV might be the fact that it is seen as an incurable lethal illness. It is important to note here that the media has its share of responsibility in the stigma against HIV, and that was also noted by health professionals in our study. The media had adopted a mechanism that seemed like “teaching by scaring”, and this was also found to be the same in Thailand, where it was described that the popular image of AIDS is influenced by the media, which sometimes created fear and anxiety that resulted in stigmatization of infected persons (50). Hence, although the role of the media is undeniable in terms of the general awareness it created about HIV, extreme portrayals of the illness have created unnecessary stigmatization of patients, and these should be modified and the information/education provided made more sensitive, and it seems like more positive information is now being provided by the media. Using already established community based organizations, religious organizations will in addition assist in reaching the community. HIV patient organizations have also played a big role in terms of raising awareness and fighting against stigma and discrimination and establishment of TB patient organizations would also be helpful; with involvement of ex-TB patients, and the two organizations should be able to work together.

#### **4.3.4.2. Social support**

As previously discussed, the social environment was at times a source of stigma, making treatment difficult for patients; and both felt and enacted stigma were making some patients reject social support. Non disclosure was common. Non disclosure is a cause of concern also because of possible transmission to others. But for those who disclosed their illness to families and at times relatives/neighbors, the support was very vital. From moral encouragement to financial assistance, to accompaniment for clinic visits as well as collection of drugs in some instances, families or others played an important role in ensuring that treatment was facilitated and adherence ensured. The importance of social support in enhancing TB treatment adherence has been described in studies from Ethiopia (29, 31), and outside Ethiopia (52, 53, 63). A study on adherence to ART in Ethiopia has also shown the important role of social support in adherence to ART treatment (82).

But for some patients, a sense of guilt developed when they felt the burden they exerted on their families was excessive, leading to discontinuation of treatment. Receiving support was most difficult for those who used to assume the role of being the ones providing for their family, when the role reversed and they were the ones receiving support. This was exemplified by the 20 years old female patient who used to support her parents (whose income only depended on the very small pension money that the father gets) and who had to depend on them for her costs including transport costs after being diagnosed with both TB and HIV. She described the role reversal as “damaging”, as quoted earlier.

In Ethiopia, extended families usually serve as a source of support for people, mainly in times of crisis. Patients’ screening out of some of this support because of fear of stigma makes the burden on close families worse, since it is not shared by others. Solving this problem will necessitate raising awareness about the TB as well as HIV, and will also involve devising mechanisms by which the costs related to treatment can be minimized, such as the provision of community based DOT as mentioned above, which can make patients less dependent on others.



### **4.3.5. Economic factors affecting adherence**

#### **4.3.5.1. Direct and indirect costs of treatment**

The impact of the economic burden has been partly described above, and will be briefly discussed here. Although the direct costs are minimal since patients receive both anti-TB and ART for free, although they at times had to pay for investigations such as x-rays themselves, indirect costs were multiple, and included transportation costs, costs due to loss of job mainly for patients who wait for daily jobs to come such as daily laborers, and other costs such as those related to food. What is worth noting here is that the public health centers are not the first health facilities visited for some, who had been to private clinics before, at times repeatedly for repeated infections because of advanced HIV illness, and hence join the health center with an already compromised economic status. Sagbakken also found that a lack of trust in governmental health centers as well as the stigma attached with attending such centers forced people to attend private facilities, where they spent much of their money before joining governmental centers where TB treatment is provided (104).

The question is then what can be done to assist patients. Minimizing DOT related transportation costs through the provision of community based DOT and working together with already existing NGOS to provide food and financial assistance such as covering transport costs have been discussed earlier. The impact of incentives such as food and transport money on improving adherence to chronic treatment in general has been demonstrated (53). In addition, studies from the United States have also indicated that increasing preexisting incentives and providing financial incentives improved adherence to TB treatment (60-62). Farmer also showed that, in a poor Haitian plateau where treatment was offered for free, adherence was only related to whether patients had access to supplemental income and food (35).

The feasibility of provision of incentives in our set up might be questionable, but, as mentioned earlier, working with NGOs already providing financial assistance to patients might be one option.

#### **4.3.5.2. Lack of food**

One factor threatening the belief in curability of TB by taking anti-TB treatment for some patients was the belief in the necessity to get good food, that is protein rich foods such as eggs and milk in order to achieve cure, and some thought of food as being as important as treatment. Patients believed that lack of food predisposed them to TB and that it will threaten their chance of getting cured. In addition, patients believed that, since they had two illnesses, and were taking many pills (anti-TB and ART); they had to take adequate food so that their body does not get harmed by the drugs; and some ascribed side effects such as gastritis to the lack of food. In addition, since patients believed in the importance of weight gain to avoid suspicion of HIV, getting food is also important for that purpose. The belief about the necessity of high protein foods while on TB treatment came from the community but also from health professionals who were informing patients on the need to consume such foods. This again is a reflection of how beliefs, emerging and reinforced by the community, the popular sector of the health care system, impact on the treatment of patients; and information provided by health professionals was also supporting these beliefs. Sagbakken similarly explains in her study from Addis-Abeba that the cultural conception, which puts emphasis on protein food, creates mental stress and hopelessness among patients, since many were actually chronically hungry, fighting to get their daily meals (104). Other studies on adherence to TB treatment and HIV treatment have similarly shown that lack of food is a barrier to treatment adherence in resource constrained set ups (51, 74, 83 ).

Health professionals should be aware that giving information about consumption of high protein diet in a set up where most of the patients can not afford such meals can be dangerous, and patients should rather be encouraged to consume whatever food is available for them, and advised to eat nutritious meals if and whenever possible. This information should also be disseminated to the community at large. One of the most common answers from patients when asked what could be done to facilitate medication intake for patients in their situation was provision of food. Many NGOs are working in Addis-Abeba to provide assistance for HIV patients. According to information I gathered from health professionals, some NGOs have criteria for deciding which patients they

would help such as the BMI of patients to provide food. In addition, patients with other chronic illness such as TB in addition to the HIV should be considered for assistance since that would facilitate their medication intake, and clinics should work in collaboration with NGOs to assist such patients.

## **Chapter five: conclusion**

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The default rate from TB treatment in this study was 10.5% (10.7% in smear positive cases); which, although still high, was less than we actually expected. WHO recommends that the rate should be less than 10% (15). The Stop TB Partnership's target for TB control, which includes achieving cure in 85% of infectious TB cases, has not been reached. Default was higher in the co-infected patients than in a comparative group of HIV negative patients that we took, but the difference was not statistically significant. We also found that many of those who manage to finish treatment do so with many challenges and struggles. We found that sex, education and timing of ART initiation were associated with defaulting from treatment from the quantitative study, and the qualitative study further showed that misperceptions existed about TB and TB/HIV, and that adverse perception of prognosis with a desire to get cured, and support from family and health professionals were assisting patients with their treatment whereas pill burden, side effects, lack of food, stigma and economic burden of treatment were making treatment difficult. We also found that proper health education/communication was not given to patients by health professionals and that TB/HIV collaborative activities were weak. Much needs to be done to make medication intake better and easier for this group of patients. Although some of the factors that make medication intake difficult in these patients are related to socio-economic factors such as poverty, which are difficult to deal with, other factors are amenable to change. We have pointed out the importance, among other things, of thorough health Information, Education and Communication to increase awareness about TB/HIV and their treatments and combat stigma, as well as the need to strengthen collaborative TB/HIV activities. We have suggested the importance of community based DOT, as well as provision of food and small financial incentives, in collaboration with existing NGOs. It is also important that health professionals be aware of facilitators and barriers to treatment in these patients and act accordingly, such as discussing thoroughly the timing of ART initiation with patients who should make informed decisions, and proper adherence counseling is mandatory. The continuation phase is a critical phase for adherence and health professionals should be aware of it and provide continuous support for patients.

Although we focused in this study on adherence to TB treatment, we actually addressed ART treatment indirectly in co-infected patients, and it seems like many patients give up both their anti-TB and ART treatments in many cases; hence the implications also extend to ART treatment. Many of the challenges such as for e.g. pill burden, side effects are also faced by patients who need to take other long term treatments in addition to their ART, and thus the findings to some extent apply to them as well.

### **Implications for further research**

1. We recommend that further prospective studies with larger sample size should be conducted, with recording of all factors potentially affecting adherence at the beginning of the study as well as the recording of factors during treatment (such as side effects) that can influence adherence in co-infected patients and follow patients subsequently
2. Similar studies should be conducted in other regions, in particular rural regions where ART is now being scaled up, to look at context specific factors influencing adherence in co-infected patients on concomitant treatment
3. Studies assessing the impact of community based DOT in regions where it is being implemented are necessary to be able to derive evidence based lessons from these areas
4. Studies looking in depth at gender differences in TB/HIV treatment are needed, which address factors such as gender differences in accessing health care and in following treatment as well as gender differentials with regard to stigma related with TB/HIV
5. Despite several reports of it, HIV related stigma in Ethiopia remains unexplored and studies addressing this issue are highly needed

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## 7. ANNEX

### ANNEX I: Form for record review

Age:            years

Sex: 0. male

1. female

Marital status: 0.single

1 .married

2. Divorced

3. Widowed

Education: 0.illiterate

1. can write and read

2. primary

3. secondary

4. higher education

Occupation:

Monthly income:     ETB

WHO stage: III

IV

Site: 0.pulmonary

1. extra pulmonary

Bacilloscopy: 0.positive

1. Negative

CD4: 0. <50

1. 50-200

2. >200

ART initiated: 0.before start of anti TB

1. in intensive phase of anti TB

2. in continuation phase of anti TB

ART regimen: 0.stavudine/lamivudine/nevirapine

1. stavudine/lamivudine/efavirenz
2. combivir/nevirapine
3. combivir/efavirenz
4. other

PCP prophylaxis: 0. yes

1. No

Other concomitant illness: 0.yes

1. No

If yes, specify

Side effect to anti TB: 0.yes

1. No

If yes, specify

Side effect to ART: 0.yes

1. No

If yes, specify

Treatment outcome: 0.cured

1. Completed treatment
2. died
3. failed
4. defaulted
5. transferred out
6. lost to follow



## **ANNEX II: Interview guide for patients**

1. How old are you?
2. What is your job?
3. Are you married?
4. Do you have children?
5. Can you estimate your monthly income for me?
6. When were you diagnosed with TB and with HIV?
7. Tell me about your illnesses (HIV/TB)?

How did the illnesses first start?

What did you then do or whom did you consult?

How did you feel when you were told about the illnesses?

8. Tell me what you know about TB?
9. Tell me what you know about HIV?
10. Do you think there is a relationship between TB and HIV?
11. If yes, what do you think is the relationship between them?
12. Tell me about your experience taking the TB medications?
13. What is/was difficult for you taking the medications?

Probe on: costs, side effects, pill burden, stigma, attitude of health personnel, effects of drug intake on daily routines, DOT, waiting times at the clinic...

14. What made it easier/assisted you with taking the medications?

Probe: belief on efficacy of treatment, social support, health professional support...

15. What impact has being HIV positive had on your TB treatment?

Probe: perception of prognosis, efficacy of treatment, stigma...

16. How about the concomitant intake of ART?

Probe on: Pill burden, perception of side effects...

17. What was your experience like as a patient in the TB and in the ART clinics?

Probe: attitude of health personnel, communication with health personnel, information received from health personnel, attitude towards DOT, collaboration between the clinics...

18. What do you think can be done for patients to facilitate medication intake in this situation?

## **ANNEX III: Interview guide for health professionals**

1. How old are you?
2. What is your occupation?
3. What is your education?
4. How long is your work experience?
5. Tell me about TB/HIV co-infection in your set up?
6. What are the common problems you encounter in patients with co-infection?
7. From your experience, is non-adherence to tuberculosis treatment in patients with co-infection a common problem?
8. What are barriers to adherence in these patients, from your experience?
9. What factors facilitate adherence in these patients, from your experience?
10. How do you assist patients with their adherence to treatment?
11. How is the collaboration between TB and HIV clinics?
12. How do you see the interaction between patients and health professionals here?
13. Do you believe patients are receiving necessary information about their illness and their treatment?
14. What strategies do you believe would assist patients with their adherence to treatment?

## **ANNEX IV: Request for participation**

### Introduction

My name is Mekdes Kebede. I'm doing a master in international health in Norway and this research is part of my study. I'm conducting interviews to find out issues related to tuberculosis medication adherence.

I would like to have a discussion with you about your experiences taking tuberculosis medications. We may need to meet again to clarify issues that might arise from our discussion. Your identity will be treated with confidentiality and the information that you provide will be used solely for the purpose of the study.

Your name will not be written on the interview note or anywhere else and will never be used in connection with any of the information you tell me. You don't have to discuss issues that you do not want to and you may end the interview any time. If you want to withdraw from the study any time along the study process you will not be obliged to continue or give reasons for doing so.

Refusing to participate or withdrawing from the study along the process will not have any consequences on you. However, the information that you provide during the discussions will help understand issues related to tuberculosis medication adherence and might help for future interventions.

The findings of the interviews might get published and contribute to understanding of barriers and facilitators of tuberculosis medication adherence in Ethiopia.

I would greatly appreciate your help in responding to the interview. If you have any questions or any thing that is not clear please feel free to ask me when we meet for the interviews.

If you are clear with the information provided and agree to participate, please inform the health professional and we shall meet at the time of your convenience for the interview.

## **ANNEX V :Consent Form**

I the undersigned has been informed that the purpose of this research is to find out issues related to tuberculosis medication adherence in Ethiopia.

I have been informed that I am going to have discussions with the researcher about issues related to tuberculosis medication adherence and that the discussion might be repeated, if there is a need to clarify issues that might arise from the discussion.

I have also been informed that the information that I give will solely be used for this study and the findings may get published, but that my identity will be treated with confidentiality and my name will not be used in connection with the information that I gave.

I have also been informed that I can refuse to discuss issues that I don't want to discuss and can stop the interview any time I want, and that I will not be obliged to continue to participate in the study or give reasons for doing so.

I have also been informed that I can stop participating any time along the study process and that refusing to participate or withdrawing from the study will not have any consequences on me.

I agree to participate in this research.

Signature -----

Date -----



